IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re <i>Inter Partes</i> Review of:)
U.S. Patent No. 5,665,772)
Issued: Sept. 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

DECLARATION OF WILLIAM L. JORGENSEN PH.D. IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 5,665,772



TABLE OF CONTENTS

		<u> </u>	<u>Page</u>
I.	Introd	duction And Qualifications	1
II.	-	Relevant Experience With Rapamycin And Other unosuppressants In The Early-1990s	3
III.	Unde	erstanding Of The Governing Law	4
	A. B.	Invalidity by Obviousness	4
IV.	Over	view Of The '772 Patent	6
	A.	Disclosure of the '772 Patent	6
V.	Prose	ecution History	14
VI.	Level	l Of Skill In The Art	15
VII.	Clain	n Construction	17
VIII.	Sumr	nary Of Opinions	17
IX.	TECI	HNICAL BACKGROUND AND SCOPE OF THE PRIOR ART	25
	A.	Background and State of the Prior Art	26
		Art	26
		2. Rapamycin's Poor Solubility Was Extremely Well-Known to Those of Ordinary Skill in the Art	27
		3. Routine Molecular Modifications To Improve Solubility Were Well-Known to Those of Ordinary Skill in the Art	
		4. Those of Ordinary Skill in the Art Made Routine	28
		Modifications to Rapamycin	40



		6. Standard Assays to Test Immunosuppressive Activities and Properties of Rapamycin Derivatives Were Well-	5. 6
	ъ	Known to Those of Ordinary Skill in the Art	
	В.	Prior Art Relevant to Obviousness Grounds 3 and 4	57
		Computer Based Modeling Allowed for Rapid Screening of Possible Modifications	57
X.		ns 1-3 & 8-10 Of The '772 Patent Would Have Been Obvious To	
	A Pe	rson Of Ordinary Skill In The Art	59
	A.	Ground 1: Claims 1-3 and 10 of the '772 Patent Would Have	
		Been Obvious In View of Morris, Lemke, Yalkowsky, and Van	
		Duyne and Rossmann	60
		1. A Person of Ordinary Skill in the Art Would Have	
		Selected Rapamycin as a Lead Compound	60
		2. A Person of Ordinary Skill in the Art Would Have Been	
		Motivated to Modify Rapamycin to Improve Its	
		Solubility As Taught in the Prior Art	63
		3. A Person of Ordinary Skill in the Art Would Have Been	
		Motivated to Select C40 of Rapamycin for Modification	
		to Avoid Disrupting Its Activity	64
		4. A Person of Ordinary Skill in the Art Would Have	
		Modified Rapamycin to Add Short, Flexible Side Chains	
		with Solubilizing Substituents at C40	67
	B.	Ground 2: Claims 8 and 9 of the '772 Patent Would Have Been	
		Obvious In View of Morris, Lemke, Yalkowsky, and Van	
		Duyne and Rossmann, in further view of Hughes	75
		1. A Person of Ordinary Skill in the Art Would Reasonably	
		Expect that Small Solubilizing Modifications to	
		Rapamycin at C40 Would Retain Immunosuppressive	
		Activity	76
	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	78
	D.	Ground 4: Claims 8 and 9 Would Have Been Obvious to a	, 0
		Person of Ordinary Skill in the Art in October 1992	86



	1. A Person of Ordinary Skill in the Art Would Reasonably Expect that Solubilizing Modifications to Rapamycin at C40 Would Retain Immunosuppressive Activity	87
XI.	Secondary Considerations Fail To Overcome The Strong Evidence Of Obviousness	89



I, William L. Jorgensen, Ph.D. resident of Deep River, Connecticut, hereby declare as follows:

I. INTRODUCTION AND QUALIFICATIONS

- 1. I have been retained by Par Pharmaceutical, Inc. ("Par") to provide my opinions concerning certain claims of U.S. Patent No. 5,665,772 (Ex. 1001, "the '772 Patent") in support of Par's Petition for *Inter Partes* Review of the '772 Patent. I have not previously been employed or retained by Par in any capacity.
- 2. From 1967 to 1970, I attended Princeton University, where I received an A.B. in Chemistry. I then attended Harvard University from 1970 to 1975, where I received a Ph.D. in Chemical Physics. My Ph.D. supervisor was Prof. E. J. Corey, a well-known synthetic organic chemist and Nobel Laureate.
- 3. From 1975 to 1979, I served as an Assistant Professor in the Department of Chemistry at Purdue University. While at Purdue, I was promoted to Associate Professor in 1979 and Professor in 1982. From 1984 to 1987, I served as the Head of the Organic Chemistry Division at Purdue.
- 4. In 1990, I joined the Department of Chemistry at Yale University as the Whitehead Professor of Chemistry. In 2009, I became the Sterling Professor of Chemistry, the position I hold today. I additionally served as the Director of the Division of Physical Sciences and Engineering at Yale from 2009 to 2012.



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.

