UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

WOCKHARDT BIO AG Petitioner

JANSSEN ONCOLOGY, INC. Patent Owner

> Case IPR2016-01582 Patent 8,822,438 B2

DECLARATION OF MATTHEW B. RETTIG, M.D. IN SUPPORT OF JANSSEN ONCOLOGY, INC.'S <u>PATENT OWNER RESPONSE</u>

A L A R M Find authenticated court documents without watermarks at <u>docketalarm.com</u>.

DOCKET

TABLE OF CONTENTS

I.	Introduction						
	A.	Engagement1					
	B.	Background and Qualifications	1				
	C.	Compensation and Prior Testimony	4				
	D.	Materials Considered	4				
II.	Legal	Legal Standards Regarding Patentability					
III.	Technical Background						
	A.	Control of Prostate Growth and Function by Androgens7					
		1. Prostate growth and function	7				
		2. Androgen Synthesis	9				
		3. Clinical Disorders Associated with Under-Production or Over-Production of Steroids and Their Treatment					
	B.	Prostate Cancer and Its Treatment as of August 2006	21				
		1. Prevalence, Diagnosis, and Early Stage Treatment	21				
		2. First Line Hormonal Therapy for Metastatic Prostate Cancer	22				
		3. Metastatic Castration Resistant Prostate Cancer	23				
	C.	Endpoints for Evaluating Response to Prostate Cancer Treatment	26				
IV.	The '	'438 Patent and its claims					
V.	Claim Construction						
VI.	Perso	Person of Ordinary Skill in the Art					
VII.	The Prior Art Relied On by Petitioners						
	A.	Gerber (Exhibit 1004)					
	B.	O'Donnell (Exhibit 1005)	37				
	C.	Sartor (Ex. 1006)	39				

VIII.	Rebuttal to Dr. Godley's Opinions Concerning Obviousness							
	A.	There Was No Scientific Basis in the Prior Art to Add Prednisone to Abiraterone Acetate for Purposes of Glucocorticoid Replacement						
		1.	As of August 2006, a POSA Would Understand that Abiraterone Acetate's Mechanism of Action and Hormonal Side Effects Were Very Different from Ketoconazole					
		2.	As of August 2006, a POSA Would Understand that Abiraterone Acetate Did Not Cause Clinical Symptoms Associated with Adrenal Suppression and Maintained Normal Cortisol Levels					
			a. O'Donnell teaches that abiraterone acetate did not have any significant effect upon cortisol levels in patients					
			b. A POSA Would Have Concluded from the Prior Art as a Whole that Abiraterone Acetate did not Cause Any Clinical Symptoms Requiring Glucocorticoid Replacement					
		3.	As of August 2006, a POSA Would Understand that Gerber's Use of "Glucocorticoid Replacement" with Ketoconazole Did Not Apply to Abiraterone Acetate					
		4.	As of August 2006, a POSA Would Not Have Given Glucocorticoids to Prostate Cancer Patients Unless There Was a Clear Clinical Need Because of Their Known Severe Side Effects and their Potential to Fuel the Cancer 57					
	B.		Was No Scientific or Clinical Basis in the Prior Art to Add Prednisone to erone Acetate to Address Mineralocorticoid Excess					
		1.	As of August 2006, a POSA Would Understand that Ketoconazole Did Not Cause Mineralocorticoid Excess Syndrome or Symptoms of Hypertension, Hypokalemia, or Fluid Retention					
		2.	As of August 2006, Nothing in the Prior Art Would Have Suggested to a POSA that Abiraterone Acetate Would Cause Mineralocorticoid Excess 68					
		3.	Even if Mineralocorticoid Excess Was Observed, As of August 2006, a POSA Would Understand that It Could Be Managed Without Glucocorticoid Replacement					
	C.	Abirat	Was No Scientific or Clinical Basis for Believing that the Combination of erone Acetate and Prednisone Could Be Successful in Achieving the ions Claimed in the '438 Patent Based on Gerber and/or Ketoconazole73					
		1.	As of August 2006, the Prior Art Did Not Teach that Ketoconazole was "Safe and Effective" for the Treatment of mCRPC73					

	D.	The Prior Art Did Not Provide a Scientific or Clinical Basis for Believing that Prednisone Would be Effective for Treating Cancer Based on Sartor and/or the State of the Art					
		1.	Sartor Did Not Establish that Prednisone "Treats Prostate Cancer				
		2.	No Other Prior Art Cited by Wockhardt Established that Glucocorticoids, Including Prednisone, Were Effective for Treating Prostate Cancer90				
			a.	Prior Art Describing Single-Agent Use of Glucocorticoids, Such as Prednisone, Did Not Demonstrate Prednisone Was Effective Treatment for Prostate Cancer	s an		
			b.	Prior Art Describing Use of Prednisone with Ketoconazole Glucocorticoid Replacement Does Not Demonstrate Prednisone Was an Effective Treatment for Prostate Canc			
			с.	Glucocorticoids, including prednisone, were used with chemotherapy agents for managing side effects that would occur with abiraterone acetate, not for "treating" prostate cancer	:		
IX.	Real World Facts Or "Objective Indicia of Non-Obviousness" Support the Non- Obviousness of the '438 Patent Invention104						
	A.	The Invention Claimed in the '438 Patent Resulted in Unexpected Clinical Efficacy					
	B.	The Invention Claimed in the '438 Patent is Embodied in ZYTIGA® Therapy and Contributes Significantly to the Success of ZYTIGA®					
	C.	Long Felt But Unsolved Need					
	D.	Skepticism and Failure of Others					
		1.	The	O'Donnell Studies	119		
		2	Othe	r Failed Phase III Clinical Trials	120		

I, Matthew B. Rettig, M.D., hereby declare as follows:

I. INTRODUCTION

A. Engagement

1. I have been retained by counsel for Patent Owner Janssen Oncology Inc. ("Janssen") to provide expert and testimony as background for the panel of Administrative Patent Judges of the Patent Trial and Appeal Board of the United States Patent and Trademark Office ("Panel") as it considers issues relating to the patentability of U.S. Patent No. 8,822,438 (the '438 Patent) (Ex. 1001) in an *inter partes* review requested by Wockhardt Bio AG (hereinafter "Wockhardt") in Case No. IPR2016-01582.

B. Background and Qualifications

2. I am Medical Director of the Prostate Cancer Program of the Institute of Urologic Oncology at the David Geffen School of Medicine at the University of California, Los Angeles ("UCLA School of Medicine"). I am also Professor in the Department of Medicine and the Department of Urology at the UCLA School of Medicine. I am also Chief of the Division of Hematology-Oncology for the Veteran's Administration (VA) Greater Los Angeles Healthcare System in West Lost Angeles. In addition, I serve as the Director of the Operation Mend Project to Enhance Cancer Care for Veterans, a collaboration between UCLA and the VA Greater Los Angeles Healthcare System to enhance cancer care for veterans.

Find authenticated court documents without watermarks at <u>docketalarm.com</u>.

DOCKET A L A R M



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.