UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE PATENT TRIAL AND APPEAL BOARD Amerigen Pharmaceuticals Limited and Argentum Pharmaceuticals LLC Petitioners V. Janssen Oncology, Inc. Patent Owner U.S. Patent No. 8,822,438 to Auerbach et al. Issue Date: September 2, 2014 Title: Methods and Compositions for Treating Cancer Inter Partes Review No. 2016-002861

Declaration of Dr. Richard I. Dorin

I declare that all statements made herein on my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Richard I. Dorin, M.D.

Date

AMERIGEN 1093



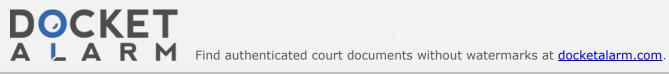
¹ Case IPR2016-01317 has been joined with this proceeding.

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	AA administered to humans inhibits BOTH 17-hydroxylase and 17,20-lyas ivities.	
in t	Among the spectrum of P450c17 deficiency syndromes related to mutation the P450c17 gene, the subtype designated as combined, partial 17-droxylase/17,20-lyase deficiency is the most relevant and appropriate for alogy in relation to men receiving long-term AA.	
ana	I disagree with Dr. Auchus' conclusion (paragraph 58) that the relevant alogy between AA and P450c17 deficiency would be "isolated 17,20-lyase" ficiency (Auchus paragraph 58).	9
	A POSA would conclude that there is a substantial risk for clinically relevantisol deficiency in men with mCRPC treated long term with AA	
min tha	POSA would conclude that there is a substantial risk for development of neralocorticoid excess in men with mCRPC treated with long-term AA, and it "concomitant administration of replacement glucocorticoid" would be a sonable, safe, and appropriate management strategy for prevention and atment of mineralocorticoid excess.	13
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		Dr. Auchus' concern that the dose of Synacthen (1 vs. 250 μ g) used by C was not specified is invalid but, regardless, would not influence repretation of Δ -cortisol data	
	-	Dr. Auchus' concern that time of day that the Synacthen test was formed was not specified is invalid but, regardless, would not influence repretation of Δ -cortisol data	
	addi	Dr. Auchus argument (paragraph 28) that O'Donnell presentation of isol data in Study should have included peak cortisol instead of or in ition to Δ -cortisol is sustained, but the omission of peak cortisol centration data does not invalidate or influence POSA's interpretation	
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D. Endocrine data for single dose studies (Studies A and B) in O'Donnell would				
not dissuade a POSA from the conclusion that "adrenocortical suppression may				
necessitate concomitant administration of replacement glucocorticoid" in patients				
treated with long-term AA40				
E. The absence of overt manifestations of adrenal insufficiency during clinical				
event monitoring data reported in O'Donnell ("Overall Toxicity" section) would				
not dissuade a POSA from the conclusion that "adrenocortical suppression may				
necessitate concomitant administration of replacement glucocorticoid" in patients				
treated with long-term AA				
F. The absence of overt manifestations of mineralocorticoid excess during				
clinical event monitoring data reported in O'Donnell ("Overall Toxicity" section)				
would not dissuade a POSA from the conclusion that concomitant administration				
of replacement glucocorticoid is indicated in patients treated with long-term AA				
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I, Richard I. Dorin, M.D., do hereby declare:

I. Introduction

- 1. At the request of Petitioners Amerigen Pharmaceuticals, Ltd. and Argentum Pharmaceuticals, LLC ("Petitioners") in the matter of the *inter partes review* of U.S. Patent No. 8,822,438 (the "'438 Patent" (AMG 1001), requested by Petitioners and instituted by Patent Trial and Appeal Board of the United States Patent and Trademark Office in Case No. IPR2016-00286 and Case No. IPR2016-01317, I have been asked to provide my opinions regarding the expert declaration and deposition testimony of Richard Auchus, M.D., Ph.D., submitted on behalf of Patent Owner Janssen Oncology, Inc. ("Janssen").
- 2. I am being compensated for my work in this matter at the rate of \$400.00 per hour. My compensation in no way depends on the outcome of this proceeding. The opinions I set forth herein are my own, and are based on the education, experience, training and skill that I have accumulated in the course of my career as a physician and researcher, as well as the materials I have reviewed in connection with this case.

II. Education and Professional Background

3. I currently practice medicine at the New Mexico Veterans

Administration Healthcare System in Albuquerque, New Mexico. I am also a

Professor of Medicine and Biochemistry & Molecular Biology at the University of



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