UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE PATENT TRIAL AND APPEAL BOARD ______

ELI LILLY AND COMPANY Petitioner,

V.

TEVA PHARMACEUTICALS INTERNATIONAL GMBH Patent Owner

Case IPR2018-01427 Patent 8,597,649 B2

DECLARATION OF DR. MICHEL D. FERRARI, M.D., PH.D.



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VII.	My Understanding of Obviousness
	Before November 2005, the field was focused on treating acute migraine small molecule therapeutics with short half-lives
	Dr. Charles and Dr. Vasserot ignored the potentially life-threatening side s of long-term antagonism of CGRP's normal function
_	Problems in the vascular system can lead to life-threatening situations20 Because of CGRP's potent vasodilatory properties, a POSA would have ected that sequestering CGRP would risk serious negative consequences to a lent's vascular health
1	
2 is	A POSA would have expected that sequestering CGRP would risk serious schemic episodes
3 b	. A POSA would have expected that sequestering CGRP would lead to high lood pressure and its associated risk of heart disease and stroke
_	Anti-CGRP antibodies would have presented an even greater risk for graineurs because of an established comorbidity of migraine with stroke and diac infarcs
D. effe	Tan 1995 did not demonstrate that a full length antibody could be safe or ective for clinical use in patients39



Inter Partes Review of USPN 8,597,649 Declaration of Michel D. Ferrari, M.D., Ph.D. (EX2141)

	Lassen did not demonstrate that an anti-CGRP antibody could be safe or ective for clinical use in patients	
	Experiments with BIBN4096BS had not demonstrated that anti-CGRP odies were suitable for or safe in human patients	.43
were	Contrary to Dr. Charles's and Dr. Vasserot's assertions, CGRP antibodies not known treatment options for CGRP-mediated diseases prior to Novemb	er
	Dr. Charles's and Dr. Vasserot's arguments are particularly flawed with ct to claims 8 and 9	.51
XIII.	Anti-CGRP antibodies demonstrated unexpectedly superior results	.53
XIV.	Humanized anti-CGRP antibodies faced industry skepticism	55



Inter Partes Review of USPN 8,597,649 Declaration of Michel D. Ferrari, M.D., Ph.D. (EX2141)

I, Michel D. Ferrari, M.D., Ph.D., hereby declare as follows.

I. Introduction

- 1. I have been retained as an expert witness on behalf of Teva Pharmaceuticals International GMBH ("Teva") for the above-captioned *inter partes* review (IPR). I am being compensated for my time in connection with this IPR at my standard consulting rate, but my compensation is not contingent upon my opinions or the outcome of this or any other proceeding.
- 2. I understand that this Declaration accompanies Teva's response to an IPR petition involving U.S. Patent No. 8,597,649 ("the '649 patent") (EX1001). I understand that the petition was filed by Eli Lilly and Company ("Lilly"). I understand that the '649 patent resulted from U.S. Patent Application No. 13/870,871 ("the '871 application"). I understand that the '871 application is a continuation application that relates to a series of previous applications. I also understand that the earliest possible priority date of the '649 patent is the November 14, 2005 filing date of U.S. Patent Application No. 60/736,623, and I refer to this date throughout this declaration. The '649 patent issued on December 3, 2013.
- 3. In preparing this Declaration, I have reviewed the '649 patent and each of the documents cited herein from the perspective of a person of ordinary



skill in the art, in light of general knowledge in the art before November 14, 2005. In formulating my opinions, I have relied upon my experience, education, and knowledge in the relevant art. In formulating my opinions, I have also considered the viewpoint of a person of ordinary skill in the art ("POSA") (*i.e.*, a person of ordinary skill in the field of the '649 patent, as defined further below in Section V) prior to November 14, 2005.

II. My Background and Qualifications

- 4. My qualifications and credentials are more fully set forth in my *curriculum vitae*, provided as EX2142. I am an expert in the field of clinical neurology, and have been since approximately 1985. I have been actively working in the field of neurology, with a focus on migraine, since 1980, and have gained significant experience in this field while both performing clinical research and treating patients since I graduated from medical school.
- 5. I studied medicine at the University of Leiden and received my Doctor of Medicine Degree in 1980. I subsequently decided to specialize in Neurology and Neuroscience and received specialty certificates in Neurology and Clinical Neurophysiology in 1985. I was awarded a Ph.D. *cum laude* in 1992 and the title of my thesis was "Serotonin and Migraine,"
- 6. I have dedicated much of my career to the study of migraine and other primary headaches and the focus of my research has been aimed at unravelling the



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