Case IPR2018-01425 Patent No. 9,890,210

IN THE 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 IPR2018-01425 Patent 9,890,210 B2

TEVA PHARMACEUTICALS INTERNATIONAL GMBH'S PATENT OWNER RESPONSE

Mail Stop "PATENT BOARD"

Patent Trial and Appeal Board U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313-1450

DOCKET

TABLE OF CONTENTS

I. Intr	oduction	1
II. Bao	ckground	8
A.	Calcitonin Gene-Related Peptide ("CGRP")	8
B.	The '210 patent and its commercial embodiments	9
	POSA would not have had a reason to humanize anti-CGRP ibodies as of 2005	1
A.	Lilly's reasons to combine the art as claimed are based on "therapeutic use in humans" of humanized anti-CGRP antibodies	1
В.	Lilly mischaracterizes what the cited art would have conveyed to the POSA	4
	1. Tan 1995 provided no "guidance" about treating vasomotor symptoms with anti-CGRP antibodies in humans	4
	2. Lilly's experts internally disagree on what the cited art discloses	5
	3. Wimalawansa provided no guidance to humanize anti- CGRP antagonist antibodies without conducting further studies	7
C.	Lilly ignored the known potentially deleterious effects of anti- CGRP antibodies in its "motivation" analysis2	0
	1. As of 2005, CGRP was known to have an important vasoprotective role in humans	1
	2. Tan 1995 and Wimalawansa also raised substantial safety concerns, which Lilly ignored	2
	3. Migraine patients present even greater safety concerns with using antibodies, which Lilly failed to address 2.	5

Case IPR2018-01425 Patent No. 9,890,210

		4. Lilly's cited art does not overcome the known safety concerns associated with anti-CGRP antibodies in 2005 27
	D.	The safety concerns that Lilly overlooked provide reasons a POSA would <i>not</i> have humanized an anti-CGRP antibody
IV.	A PO	SA would not have had a reasonable expectation of success
	A.	A POSA would not have had a reasonable expectation of success because Tan 1995 shows that the full-length antibody was not successful at achieving immunoblockade
	B.	Tan's speculation would not persuade a POSA of therapeutic success in view of Tan's demonstrated potential for side effects38
V.		's obviousness case is the product of hindsight, driven only by plution provided in the '210 patent
VI.		g objective evidence compels finding non-obviousness of the enged claims
	A.	The challenged claims have a presumption of nexus to the objective indicia of nonobviousness
	B.	The claimed humanized anti-CGRP antibodies have received industry-wide acclaim
	C.	Humanized anti-CGRP antibodies satisfied long-felt, unmet need
	D.	Humanized anti-CGRP antibodies achieved unexpected results50
	E.	Humanized anti-CGRP antibodies faced industry skepticism
	F.	Commercial success reinforces the non-obviousness of the claimed invention
	G.	AlderBio's decision to take a royalty-bearing license to Teva's patents supports nonobviousness
	H.	Lilly's simultaneous invention argument is not supported by the facts or the law

VII.	Lilly has failed to carry its burden so the Board must find for Patent Owner	55
VIII.	Conclusion	56
CERT	TIFICATE OF WORD COUNT (37 C.F.R. § 42.24(d))	57
CERT	TIFICATE OF SERVICE (37 C.F.R. § 42.6(e))	58

Teva Pharmaceuticals International GmbH ("Teva") submits this Patent Owner Response to the Petition for *Inter Partes* Review ("IPR") of U.S. Patent No. 9,890,210 filed by Eli Lilly and Company ("Lilly"). Teva's Response is supported by the expert declarations of Michel Ferrari, Ian Tomlinson, Steven Foord, Alan Rapoport, and Robert Stoner. EX2213, ¶¶4-11; EX2225, ¶¶4-9; EX2231, ¶¶4-13; EX2236, ¶¶4-11; EX2242, ¶¶1-4. This filing is timely under 35 U.S.C. §§ 311-19 and 37 C.F.R. § 42.120.

I. Introduction

The challenged claims recite novel *humanized* anti-Calcitonin Gene-Related Peptide ("CGRP") antagonist¹ antibodies useful in the treatment of various vasomotor-related ailments, including migraine. Patent Owner Teva's discovery was a breakthrough, representing the first time that *anyone, anywhere* in the world developed a humanized anti-CGRP antibody that could successfully be used as a human therapeutic. As a result, Teva's Ajovy® (fremanezumab-vfrm)—the first commercial embodiment of the challenged patent claims—when approved, was the

¹ Antagonism is achieved when a molecular blocker inhibits receptor signaling. EX2231, ¶21.

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.