IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ELI LILLY AND COMPANY,
Petitioner,

v.

TEVA PHARMACEUTICALS INTERNATIONAL GMBH,
Patent Owner.

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Case IPR2018-01422 (Patent 9,340,614 B2)
Case IPR2018-01423 (Patent 9,266,951 B2)
Case IPR2018-01424 (Patent 9,346,881 B2)
Case IPR2018-01425 (Patent 9,890,210 B2)
Case IPR2018-01426 (Patent 9,890,211 B2)
Case IPR2018-01427 (Patent 8,597,649 B2)[1]

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**PATENT OWNER'S DEMONSTRATIVES**

[1] A word-for-word identical copy of this paper is filed in each proceeding identified in the caption.

teva

2018-01422
2018-01423
2018-01424
2018-01425
2018-01426
2018-01427

Sterne Kessler

# Eli Lilly and Company
# v.
# Teva Pharmaceuticals International GmbH

November 22, 2019

# A POSA would not have had a reason to humanize anti-CGRP antibodies with a reasonable expectation of success POR, 4-5, 10-12, 19-22, 36-40 , 46-51

**Tan 1995's full-length antibody did not achieve immunoblockade:**

- "**only the Fab' fragment** was found to be an effective tool for blockade " in rats. EX1022, 570; POR, 39; EX2054, ¶51.

**Wimalawansa's reference to anti-CGRP antibodies is inconclusive:**

- "Clearly, more data from carefully designed studies are necessary before any definitive conclusions can be reached and before CGRP antagonist, **humanized anti-CGRP monoclonal antibodies**, or both, can be evaluated as therapeutic agents in humans." EX1096, 567; POR, 4, 7, 10-11, 19-22; EX2137, ¶¶80-85; EX2054, ¶¶56-59; EX2141, ¶¶25, 72.
- "These data warrant further studies in an animal model of sepsis to determine whether ***blocking CGRP receptors with specific antagonists or monoclonal antibodies*** has beneficial effects on the outcome." EX1096, 568; POR, 10-11, 49; EX2054, ¶58; EX2241, ¶86.

**The decade between Tan/Wimalawansa and Teva's invention:**

- Salmon, Sveinsson, and the '438 patent mention anti-CGRP antibodies in passing and provide no data. POR, 34-36; EX1026, 7:19; EX1027, ¶[0038]; EX1028, 2:17-55.

# Before Teva's invention, the industry focused on receptor antagonists and triptans POR, 10-11, 49

**Wimalawansa:**

- "CGRP antagonists can be used in the late phase [of migraine]. However, ***the antagonist must be extremely specific to the CGRP receptors*** located in cerebral arteries to avoid potential deleterious side effects caused by blocking other vascular and nonvascular CGRP receptors." EX1096, 568; POR, 11, 20, 49; Institution Decision, 15; EX2241, ¶86
- "These data warrant further studies in an animal model of sepsis to determine whether ***blocking CGRP receptors with specific antagonists or monoclonal antibodies*** has beneficial effects on the outcome." EX1096, 568; POR, 10-11, 49; EX2054, ¶58

**Arulmani:**

- "An important breakthrough in the field of CGRP receptors is the ***development of potent CGRP receptor antagonists.***" EX1031, 323; POR, 49; EX2141, ¶23

**Olesen:**

- "BIBN 4096 BS is a nonpeptide ***CGRP-receptor antagonist*** with an extremely high affinity and specificity for the human CGRP receptor." EX1025, 1105; POR, 49; EX2141, ¶22

**Arulmohzi:**

- "The last decade has witnessed the ***advent of Sumatriptan and the 'triptan' class of 5-HT$_{1B/1D}$ receptor agonists*** which have well established efficacy in treating migraine." EX1040, 176; POR, 49; EX2141, ¶21

# Teva's invention led to breakthrough migraine therapy POR, 52-56

**Lilly admits that the claimed antibodies satisfied a long-felt, unmet need:**

- Humanized anti-CGRP antibodies are a: "[s]afe, effective and well tolerated treatment for the prevention of migraine" that satisfied this "enormous unmet medical need." EX2161, 6; POR, 55-56; EX2165, ¶¶25-44

**The Industry praised the claimed antibodies:**

- "an enormous step forward" EX2172, 1-2; POR, 52-55; EX2165, ¶50
- "a game changer" EX2179, 4; POR, 52-55; EX2165, ¶52
- a "breakthrough in migraine" EX2174 ,707; POR, 52-55; EX2165, ¶49

**Lilly's expert, Dr. Charles, also praised the claimed antibodies as:**

- "radical concept" EX2053, 23; POR, 52-55; EX2165, ¶57
- "very exciting and compelling" EX2182, 207; POR, 9; EX2165, ¶57
- "absolutely life-changing" EX2186, 4; POR, 52-53; EX2165, ¶57
- "spectacular" EX2186, 4-5; POR, 52-53; EX2165, ¶57

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