UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

TEVA PHARMACEUTICALS INTERNATIONAL GMBH and TEVA PHARMACEUTICALS USA, INC.,	*	
Plaintiffs,	*	Civil Action No. 18-cv-12029-ADB
v.	*	
ELI LILLY AND COMPANY,	*	
Defendant.	*	

MEMORANDUM & ORDER ON CROSS-MOTIONS FOR SUMMARY JUDGMENT

Plaintiffs Teva Pharmaceuticals International GmbH and Teva Pharmaceuticals USA, Inc. (collectively, "Teva") and Defendant Eli Lilly and Company ("Lilly"), competing pharmaceutical companies, have both developed antibodies capable of treating headache disorders associated with calcitonin gene-related peptide ("CGRP"). In the instant case, Teva alleges that Lilly has infringed three of its patents[1] (the "Patents-in-Suit"), seeks a declaration that Lilly is judicially estopped from raising arguments that conflict with arguments it made in prior *inter partes* review ("IPR") proceedings, and argues that Teva does not have unclean hands or engage in inequitable conduct. Lilly, in turn, seeks declarations that its product, Emgality®, also known as Galcanezumab, does not infringe the patents, willfully or otherwise, and that the asserted patents are invalid under 35 U.S.C. § 112.

[1] U.S. Patent Nos. 8,586,045 (the "'045 patent"); 9,884,907 (the "'907 patent"); and 9,884,908 (the "'908 patent").

I. FACTUAL BACKGROUND

After weeding through the more than 1,296 pages of asserted facts and responses, the following facts are undisputed except where otherwise noted.

A. Migraine, Headache Disorders & CGRP

"Migraine is a common chronic, recurrent neurological disorder that affects greater than 10% of adults globally and approximately 39 million individuals in the United States." [ECF No. 400 ¶ 106 (citation omitted)].[2] It is among the more than 200 classifications of headache disorders listed by the International Classification of Headache Disorders, 2nd edition. [Id. ¶ 110].

CGRP is a neuropeptide that, as of 2005–2006,[3] was understood to be involved in head pain in a variety of contexts, including migraine headaches. [ECF No. 400 ¶¶ 114, P47]. At that time, CGRP had been the subject of thousands of peer-reviewed articles, [id. ¶ P46], and drugs affecting the CGRP pathway were used to treat migraine and other forms of headaches, [id. ¶ P48]. CGRP has four functional regions: (1) the N-terminal end; (2) the mid-region; (3) a hinge-like region; and (4) the C-terminal end. [Id. ¶ 113].

B. Antibodies

An antibody, or immunoglobin, is a specialized protein molecule that recognizes and binds to a target molecule known as an antigen. [ECF No. 400 ¶ 26]. "The main function of

[2] The Court draws the facts primarily from the parties' Reply Statements of Material Facts, [ECF Nos. 387 (Unclean Hands), 389 (Judicial Estoppel), 395 (Willful Infringement), 400 (Written Description), 406 (Non Infringement), and 411 (Lack of Enablement)], which contain both parties' positions on the material facts, and the documents referenced therein. The Court further notes that citations to specific paragraphs are inclusive of the response to said paragraph.

[3] The Court looks to scientific knowledge as of 2005 to 2006 because the Patents-in-Suit claim priority to Provisional Application No. 60/736,623, which was filed on November 14, 2005, and to Application No. 12/093,638, which was filed on November 2, 2006. [ECF No. 411 ¶ 142].

antibodies is to bind to antigens and neutralize them or to mark them for destruction." [Id. ¶ 48]. The portion of an antigen that is bound by an antibody is called an epitope. [Id. ¶ 27]. Antibodies themselves are made up of amino acids that are connected to each other in linear chains, often referred to as amino acid sequences. [Id. ¶ 29].

Typical full-length antibodies have four chains of amino acids: two identical heavy chains and two identical light chains. [ECF No. 400 ¶¶ 30, 32]. Each heavy chain and each light chain has a variable domain and each variable domain has three complementarity determining regions ("CDRs"). [Id. ¶¶ 31–33]. Thus, a typical full-length antibody has six unique CDRs and two unique variable domains. See [id. ¶¶ 32–33, 68, P35, P104]. The CDRs, which combine to form the variable domains, form the primary binding interface between the antibody and the epitope of the antigen, [id. ¶ 37], with the amino acid sequence of each of the CDRs causing the variable domains to adopt unique three-dimensional structures, [ECF No. 406 ¶¶ 17–18]. The amino acid sequence of the variable region differs for each antibody, [ECF No. 400 ¶ 34], and contains approximately 220 amino acid residues, [id. ¶ 35].

The number of possible permutations of antibodies is extraordinarily broad. See [ECF No. 400 ¶ 59]. The claims in the Patents-in-Suit, however, do not claim every antibody that could possibly be generated, rather they claim "a specific subset of anti-CGRP antibodies that antagonize CGRP function." [Id. ¶ 66 (quoting ECF No. 296-64 ¶ 206)]. Lilly argues that this subset of antibodies would nonetheless be extraordinarily hard to identify because "[a]s of 2005–2006 it was not possible to predict an antibody's function based on its amino acid sequence." [Id. ¶ 72]. Teva disputes this, arguing that, by that time, "it was well known that antibodies have common amino acid sequences that contribute in known ways to known functions, including antibodies generally and antibodies within particular known classes." [Id.].

C. Development of Antibodies for Therapeutics

To be safe and effective as a treatment for any type of headache disorder, an antibody must share certain general characteristics with naturally occurring human antibodies. See [ECF No. 400 ¶¶ 93–94]. If it does not, the antibody may be recognized by the body as foreign and become the target of a potentially dangerous immune response, resulting in the elimination of the antibody, a loss of therapeutic efficacy, and possibly serious allergic reactions. [Id. ¶ 93].

As of 2005–2006, one of the processes used to develop new therapeutic antibodies involved the use of murine (*i.e.*, mouse) antibodies. [ECF No. 400 ¶ 91]. These murine antibodies were generated by injecting mice with an antigen of interest, which caused the mouse to produce a type of white blood cell, referred to as B cells, that, in turn, produced a large variety of antibodies to protect against what the mouse's immune system perceived as a foreign antigen. See [id. ¶¶ 91–92]. Scientists then could isolate a B cell, fuse it to a cancer cell to form a hybrid cell known as a hybridoma, which then produced antibodies having an identical amino acid sequence (*i.e.*, "monoclonal" antibodies). [Id. ¶ 92]. An antibody produced in this way is not human, however, and to avoid human immune systems rejecting the foreign antibody, it was necessary to use genetic engineering to "humanize" the murine antibodies. [Id. ¶¶ 93–94]. This process involved replacing portions of the genes encoding the murine antibody with portions that encode a human antibody. [Id. ¶ 94]. As of 2005–2006, humanization of murine antibodies was sufficiently established to be considered "conventional" and "routine," but the parties dispute how labor intensive and time consuming the process was. See [id. ¶¶ 95–98, P8, P54, P64–66].

D. Key Antibody Attributes

To be effective in treating headache disorders caused by CGRP, an antibody produced by the methods previously described must possess several characteristics. Among the most important is its "affinity" for the target antigen, which refers to how strongly the antibody

attaches to the target. [ECF No. 400 ¶ 42]. One measure of affinity is the dissociation constant of the antibody-antigen interaction, or "K_D" value. See [id. ¶ 189]. A related property is an antibody's "neutralizing" capability, meaning its ability to inhibit the biological activities of the antigen to which it binds. [Id.]. A high affinity is integral to an antibody's neutralizing capability, otherwise the antibody will not effectively inhibit the target antigen (*e.g.*, CGRP). See [id. ¶ P67].[4]

E. The Asserted Patents and Specifications

Teva asserts twenty claims from three patents: the '045, '907, and '908 patents. See [ECF No. 400 ¶ 1; ECF No. 298 at 6]. The patents each claim the use of human or humanized anti-CGRP antagonist antibodies[5] to treat vasomotor symptoms, such as headaches. [ECF No. 400 ¶ 185–86]. The '045 patent is titled "Methods of Using Anti-CGRP Antagonist Antibodies," and the '907, and '908 patents share the title "Methods for Treating Headache Using Antagonist Antibodies Directed Against Calcitonin Gene-Related Peptide." [ECF No. 387 ¶¶ 1, 3, 5]. Named inventors for all three patents include, among others, Joerg Zeller, Kristian T. Poulsen, Yasmina Noubia Abdiche, and Jaume Pons. [Id. ¶¶ 2, 4, 6]. Each of the Patents-in-Suit claim priority to Provisional Patent Application No. 60/736,623, which was filed on November 14, 2005, and to Application No. 12/093,638, which was filed on November 2, 2006, [ECF No. 400 ¶ 183], and later published on May 18, 2007 as International Publication Number WO 2007/054809 (the "'809 application"), [ECF No. 395 ¶ P2].

[4] Teva objects to Paragraph P67, [ECF No. 400 ¶ P67], but does not dispute that antibodies that bind to the C-terminal, mid-, or N-terminal regions of CGRP can all antagonize CGRP if they exhibit high enough binding affinity and block CGRP's interaction with the CGRP receptor.
[5] The Court has construed the term "anti-CGRP antagonist antibody" as "an antibody that is able to bind to CGRP and inhibit CGRP biological activity and/or downstream pathway(s) mediated by CGRP signaling." [ECF No. 101 at 11].

i. The ’045 Patent

Teva asserts one independent claim from the ’045 patent, which recites as follows:

> 17. A method for reducing incidence of or treating headache in a human, comprising administering to the human an effective amount of anti-CGRP antagonist antibody, wherein said anti-CGRP antagonist antibody is a human monoclonal antibody or a humanized monoclonal antibody.

[ECF No. 400 ¶ 251]. The Court has previously construed the term “effective amount” to mean “an amount sufficient to effect beneficial or desired results, including but not limited to clinical results.” [ECF No. 101 at 31]. Teva also asserts seven dependent claims of the ’045 patent, [ECF No. 400 ¶ 252]: claims 18 and 21 recite specific amino acid sequences of portions of the antibodies, [id. ¶¶ 253, 256], claim 19 limits the condition treated to several specific headache disorders, [id. ¶ 254], claim 20 specifies the strength of binding, [id. ¶ 255], claim 24 limits the condition treated to migraine, [id. ¶ 257], claim 27 limits the routes of administration, [id. ¶ 258], and claim 30 requires that the anti-CGRP antagonist antibody is a humanized monoclonal antibody, [id. ¶ 259].

ii. The ’907 and ’908 Patents

Teva similarly asserts one independent claim of the ’907 patent, claim 1, which recites as follows:

> 1. A method for treating headache in an individual, comprising: administering to the individual an effective amount of a humanized monoclonal anti-[CGRP] antagonist antibody, comprising: two human IgG heavy chains, each heavy chain comprising three complementarity determining regions (CDRs) and four framework regions, wherein portions of the two heavy chains together form an Fc region; and two light chains, each light chain comprising three CDRs and four framework regions; wherein the CDRs impart to the antibody specific binding to a CGRP consisting of amino acid residues 1 to 37 of SEQ ID No:15 or SEQ ID NO:43.

[ECF No. 400 ¶ 262]. Teva has asserted five dependent claims from claim 1 of the ’907 patent: claim 4 requires that the antibody be administered intravenously or

subcutaneously, [id. ¶ 264], claim 5 limits the condition treated to one of a specific set of headache disorders, [id. ¶ 265], claim 6 limits the condition treated to migraine, [id. ¶ 266], and claim 15 specifies that the constant regions of the IgG heavy chains are IgG4 constant regions, [id. ¶ 267].

The asserted independent claim from the '908 patent, claim 1, is identical to claim 1 of the '907 patent, with the following information added to the end: "and wherein the antibody binds to the CGRP with a binding affinity (K_D) of about 10 nM or less as measured by surface plasmon resonance at 37° C." [ECF No. 400 ¶ 269]. Teva asserts five dependent claims from the '908 patent, which are identical in number and language to the dependent claims asserted in the '907 patent. [Id. ¶¶ 270–75].

iii. The Shared Specification of the Patents-in-Suit

The specifications in each of the Patents-in-Suit are substantively identical, [ECF No. 400 ¶ 184], and describe the claimed invention as "concern[ing] anti-CGRP antagonist antibodies and methods of using anti-CGRP antagonist antibodies for treating or preventing . . . headaches, such as migraine" as well as other types of headaches. [ECF No. 411 ¶ 144]. The specification (1) states that" [a]nti-CGRP antagonist antibodies are known in the art . . . ." [ECF No. 400 ¶ 204 (Teva, in response, citing the '045 patent at 25:59–61)];[6] (2) describes a full-length humanized "anti-CGRP antagonist antibody referred to as Antibody G1 and later re-named fremanezumab[,]" [ECF No. 411 ¶ 145 (citations omitted)], as well as 84 humanized anti-CGRP antibody variants of G1 ("M1-M84"), which vary from Antibody G1 by 10 or fewer amino acids,

[6] Lilly agrees that murine anti-CGRP antibodies were known in the art but disputes that humanized or human anti-CGRP antibodies were known in the art. See, e.g., [ECF No. 400 ¶ P28].

[ECF No. 400 ¶¶ 192, P103];[7] (3) discloses the complete amino acid sequence of Antibody G1, including the variable region and CDR portions of the antibody, [id. ¶ P104]; (4) discloses, in addition to the humanized antibodies, 12 murine anti-CGRP antibodies, seven of which were shown to be CGRP antagonists, [id. ¶ P102]; (5) describes "the routine methods for making humanized and human antibodies[,]" [id. ¶ P97 (citation omitted)], but does not disclose how Antibody G1, in particular, was made, [id. ¶ 188]; (6) states that by 2005–2006, methods for humanization of antibodies were well-known, routine, and reliable in the prior art and that conventional humanization techniques were routinely used that preserved the affinity and specificity of the donor antibody, [id. ¶ P64–65]; (7) discloses that there were well-known screening techniques, such as the cAMP activation assay, that allowed researchers to determine whether an antibody antagonized CGRP,[8] [id. ¶ P63]; (8) reports that Antibody G1 binds to the C-terminal end of CGRP, [id. ¶ 190]; (9) includes data on antibodies that bind to CGRP's C-terminal but do not inhibit CGRP's effects, [ECF No. 387 ¶ 22]; (10) provides instruction about how to formulate antibodies, including anti-CGRP antagonist antibodies, and various modes of administration, [ECF No. 400 ¶ P135]; (11) offers specific examples of formulations for common modes of administration and cites prior art where further detail can be found, [id.];[9]

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[7] Light chain CDR3, heavy chain CDR1, and heavy chain CDR3 of all 84 variants (M1–M84) are identical to those of Antibody G1. [ECF No. 400 ¶ 194]. Additionally, the specification does not report *in vitro* or *in vivo* experiments evaluating the ability of antibodies M1–M84 to inhibit CGRP biological activity. [Id. ¶ 196]

[8] The parties dispute whether the specification disclosed human anti-CGRP antagonist antibodies: such antibodies are not explicitly referenced, but the technology to humanize antibodies was "routine" and discussed in the specification. Compare [ECF No. 400 ¶ 205] with [id. ¶ P66, P96].

[9] Lilly purports to object to Paragraph P135, [ECF No. 400 ¶ 135], however, Lilly does not dispute that the specification includes specific examples of formulations for common modes of administration. Rather, Lilly argues that the specification "offer[s] no support to show that the inventors made anti-CGRP antibody formulations that included all possible routes of

(12) describes how anti-CGRP antagonist antibodies can be used to treat headache by administering an anti-CGRP antagonist antibody to a patient prior to, during and/or after headache, [id. ¶ P134]; and (13) reports activity of Antibody G1 in two assays conducted in rats: a saphenous nerve assay and a closed cranial window assay, [id. ¶ 214].[10]

Teva currently has an antibody product within the scope of its patents called Ajovy® (Fremanezumab), that is prescribed to treat migraine. [ECF No. 400 ¶ 375].

iv. Information Omitted from the Specification

Lilly alleges that by not disclosing certain information in the shared specification of the Patents-in-Suit, Teva engaged in inequitable conduct. [ECF No. 387 ¶ 13]. In particular, Lilly points to the fact that named inventors, Drs. Zeller and Pons, did not, in the '045 patent, disclose to the U.S. Patent and Trademark Office ("PTO") prior art literature of which they were aware, specifically, Shaw et al., *The effect of monoclonal antibodies to calcitonin gene-related peptide*

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administration in the art" and claims that "Teva's inventors testified to ***not*** having made any anti-CGRP antibody formulations for certain routes of administration known in the art." [Id.]. Neither of Lilly's assertions, however, disputes Teva's claim that the specification includes specific examples of formulations for common modes of administration.

[10] The saphenous nerve assay tests whether an anti-CGRP antibody can inhibit CGRP biological function in a live animal at a site of action relevant to migraine, whereas the closed cranial window assay measures the effect of an anti-CGRP antagonist antibody on the dilation of dural arteries, which is known to be associated with head pain. Teva asserts that a positive result in the closed cranial window assay was understood to be predictive of efficacy for treating migraine in humans, and although Lilly does not directly dispute this statement, Lilly claims the assertion is contradicted by Teva's expert who testified that "preclinical animal experiments [] will never satisfy concerns about efficacy and safety . . . ." [Id. ¶ P79]. Lilly further claims that Teva's statement is unsupported because its specification states that "the precise pathophysiology of migraine is not yet well understood." [Id.]. The Court notes that neither piece of testimony cited by Lilly actually contradicts Teva's statement and therefore finds that the Teva's assertion—that a positive result in the closed cranial window assay was understood to be predictive of efficacy—is not disputed. Teva acknowledges that the specification does not disclose any experiment involving administration of anti-CGRP antibodies to non-human primates or humans. [ECF No. 411 ¶¶ 196–97]. The parties do dispute, however, whether the results from the assay address the blood-brain barrier ("BBB"). Cf. [ECF No. 400 ¶ 219] with [id. ¶ 115].

(CGRP) on CGRP-induced vasodilation in pig coronary artery rings, 106 Br. J. Pharmacol. 196, 196–98 (1992) ("Shaw"), which taught, in part, that no antibody studied in the paper that bound to the mid-region of CGRP had blocked CGRP activity. [Id.]. Lilly further asserts that Drs. Zeller and Pons committed inequitable conduct by not disclosing to the PTO (1) the results of experiments that showed that some N-terminal antibodies bind to but, nevertheless, do not antagonize CGRP, [ECF No. 348-1 at 9]; see [ECF No. 387 ¶ 40]; (2) certain non-C-terminal binding data that addressed polyclonal antibodies, [ECF No. 387 ¶ 41; ECF No. 348-1 at 9]; and (3) data from a cortical spreading depression ("CSD") assay, [ECF No. 387 ¶ 15; ECF No. 348 at 11]. With regard to this last point, the CSD assay was, at the time, a preferred *in vivo* test used to evaluate migraine pathophysiology because it allowed researchers to, among other things, evaluate whether a drug could effect a particular migraine symptom. [ECF No. 387 ¶ 53]. Lilly claims that Dr. Pons was on notice of the importance of the test because he was on an email chain in which another scientist stated that if the anti-CGRP antibody "doesn't work" in the assay, "then the whole concept is questionable." [Id. ¶ 57 (quoting ECF No. 354-26)]. Lilly's expert Dr. Charles described the CSD assay results as "material" in his report, which, in his view, meant that the information was "germane to the patent issue." [Id. ¶ 28 (quoting ECF No. 304-18)]. The parties dispute whether the results of the CSD assay were either inconclusive because the experiment lacked a control (Teva's position) or negative (Lilly's position), and whether a negative result means that the antibody does not work to treat migraine. [Id. ¶¶ 54–56].

F. Lilly's Development of Emgality® (Galcanezumab) and Knowledge of Teva's Patents

In 2004, Lilly began a program to develop an anti-CGRP antagonist antibody for the therapeutic treatment of migraine, which eventually led to the creation of Emgality. [ECF No.

395 ¶ 21]. During this process Lilly successfully generated murine antibodies that bound to the mid-region of CGRP, screened them for CGRP antagonism, and ultimately humanized an antibody that was later named Galcanezumab. [Id. ¶¶ 28–32]. Lilly did not create Galcanezumab, however, until 2008–2009.[11] [Id. ¶ P4]. Lilly also applied for and was granted a patent (U.S. Patent No. 9,505,838 (the "'838 patent")) directed to the use of Galcanezumab to treat migraine. [ECF No. 406 ¶ 125]. Galcanezumab is the only therapeutic antibody approved by the FDA to treat episodic cluster headache. [ECF No. 411 ¶ 311].

Lilly had knowledge of the '045 patent at least as early as October 24, 2017, and knowledge of the '907 and '908 patents as early as February 6, 2018. [ECF No. 395 ¶ P1]. As discussed above, the Patents-in-Suit claim priority to the '809 application, [id. ¶ P2], which shares the same specification as the Patents-in-Suit. [Id. ¶ P3]. Lilly was aware of the '809 application as of June 7, 2011. [Id. ¶ P5].

G. Lilly's Marketing and Sale of Emgality®

Lilly has continuously made, marketed, and sold Emgality since October 2018. [ECF No. 395 ¶ P13]. Leading up to the launch in 2018, Lilly undertook a sales and marketing campaign to promote its product. See [id. ¶ P14].[12]

Lilly's campaign included spending $523.5 million on marketing between 2018 and 2020, [ECF No. 395 ¶ P14], and nearly $225 million on its U.S. Emgality sales force in that same time period, [id ¶ P15]. Internal documents also state that Lilly's focus was on "strategic objectives to 'Win' and 'Grow' the CGRP class," [id. ¶ P17 (quoting ECF No. 368-82)], and

[11] Lilly selected a lead murine antibody for humanization in April 2008, and later decided to advance the resulting humanized compound to clinical development in December 2009. [ECF No. 395 ¶ P4].

[12] Lilly raises objections to this statement of fact, but does not dispute the underlying assertion that it engaged in a marketing campaign to promote Emgality.

describe the U.S. Emgality campaign as having a "land grab" mentality at the time the product launched, [id. ¶ P18 (quoting ECF No. 368-80) (exhibit to witness deposition)]. Lilly's campaign also involved providing free samples to healthcare providers and offering increased rebates to pharmacy benefits managers to ensure that health insurance formularies would cover Emgality. [Id. ¶ P23–24].

H. Procedural Background

Teva initiated this lawsuit on September 27, 2018, claiming that Lilly infringed nine of Teva's patents. [ECF No. 411 ¶ 2]. Soon after, Lilly responded by filing a petition for IPR by the Patent Trial and Appeal Board ("PTAB") of the three Patents-in-Suit (the "Method of Treatment patents") as well as an additional six patents (the "Composition of Matter patents"). [Id. ¶¶ 3–4]. The Composition of Matter patents and the Method of Treatment patents are directed at the same type of antibodies. [Id. ¶ P3].[13]

During the Composition of Matter IPR proceedings, Lilly argued that it would have been obvious to make a humanized anti-CGRP antibody within the scope of the claims, [ECF No. 290 at 16–17], and that "by 2005, conventional humanization techniques were routinely used that preserved the affinity and specificity of the donor antibody[,]" see [ECF No. 411 ¶ P8]. Lilly further claimed that a person of ordinary skill in the art ("POSA")[14] "would have had a reasonable expectation of successfully making a humanized anti-CGRP antagonist antibody."

[13] Although Lilly objects to Teva's statement of fact, it does not dispute that the type of antibody at issue in the Composition of Matter patents (*i.e.*, human and/or humanized anti-CGRP antagonist antibodies) are also at issue in the Patents-in-Suit. See [ECF No. 411 ¶ 10].

[14] The parties agree that a person of ordinary skill in the art would have either (1) a Ph.D. in a relevant field such as immunology, biochemistry, or pharmacology, with several years of post-doctoral experience in antibody engineering, pharmacokinetics, and pharmacodynamics, or (2) an M.D. with a residency or specialty in neurology, and several years of experience studying CGRP or treating patients with a CGRP-related disease, such as migraine headaches. [ECF No. 411 ¶¶ 223–24].

[Id. ¶ P9 (citing ECF No. 368-2 at 95, 98; ECF No. 368-3 at 104–06)]. During the proceedings, Teva argued that the challenged patents represented "the first time that anyone, anywhere in the world developed a humanized anti-CGRP antibody that could successfully be used as a human therapeutic." [Id. ¶ 7 (quoting ECF No. 292-15 at 6)]. The PTAB sided with Lilly and found that the six Composition of Matter patents were unpatentable as obvious. [Id. ¶ P4]. In so concluding, it found that "anti-CGRP antagonist antibodies were well known in the art, and that the art encouraged the development of humanized anti-CGRP antibodies." [Id. ¶ P5 (quoting ECF No. 368-2 at 95)]. Teva appealed the PTAB's decision, and the Federal Circuit affirmed. [Id. ¶ 16].

The Method of Treatment patents, generally speaking, are directed to the treatment of headache disorders with antibodies that bind to CGRP and inhibit its function. [ECF No. 387 ¶ 8].[15] In the Method of Treatment IPR proceedings, Teva argued that the patents were not obvious as a POSA "would not have used a full-length antibody to treat migraine because it

[15] Lilly claims to dispute Paragraph 8 of Teva's statement of material facts, see [ECF No. 387 at 3–4], which states, "The patent claims at issue in this case are directed to treating migraines by using antibodies that bind to the peptide [CGRP] and inhibit its function." Upon review, however, Lilly's response does not raise any dispute and merely quibbles about whether CGRP is a singular peptide and repeats Lilly's argument that Teva's antibodies bind only to the C-terminal end of CGRP whereas other antibodies inhibit CGRP by binding to its middle-region or N-terminal end. [Id.]. To begin, it is not clear that Teva's statement asserts that CGRP is singular, therefore Lilly's claim that CGRP "consists of alpha and beta isoforms" does not necessarily reflect a dispute. [Id. at 4]. Moreover, even if there was a dispute, "[a] 'material fact' is one that 'might affect the outcome' of the case[,]" Intercontinental Great Brands LLC v. Kellogg N. Am. Co., 869 F.3d 1336, 1343 (Fed. Cir. 2017) (quoting Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986)), and whether CGRP is singular does not impact the Court's analysis of the issues presently before it. Teva's statement also does not make any claim as to which portion of CGRP the antibodies bind, therefore Lilly's discussion of antibodies that bind to the N-terminal and mid-region does not evidence a dispute. Lilly further argues that Teva's statement is disputed because the claims in the Patents-in-Suit are directed towards treating other headache conditions in addition to migraine. [Id. at 4]. That assertion, however, does not dispute that the facts set forth in Paragraph 8, *i.e.*, that the Patents-in-Suit pertain to the use of antibodies to treat migraine by binding and inhibiting CGRP.

would not have been expected to cross the [blood brain barrier ("BBB")]." [ECF No. 400 ¶ P18 (quoting ECF No. 296-17 at 9)]. The PTAB agreed, finding that uncertainty about whether antibodies would need to cross the BBB weighed against a reasonable expectation of success in using the claimed methods, and therefore weighed against obviousness. [Id. ¶ P20]. Lilly appealed and the Federal Circuit affirmed. [Id. ¶ P17].

The parties have now filed six cross-motions for summary judgment. Teva's motions argue that Lilly should be judicially estopped from raising arguments contrary to the positions it advanced in the IPR proceedings and that Lilly cannot succeed on its inequitable conduct claims. Lilly's motions contend that its product, Emgality, does not infringe, willfully or otherwise, the claims of the Patents-in-Suit and, alternatively, that Teva's patents are invalid for lack of written description and lack of enablement.

II. STANDARD OF REVIEW

Summary judgment is appropriate where the moving party can show that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "[A]n issue is 'genuine' if it 'may reasonably be resolved in favor of either party.'" Robinson v. Cook, 863 F. Supp. 2d 49, 60 (D. Mass. 2012) (quoting Vineberg v. Bissonnette, 548 F.3d 50, 56 (1st Cir. 2008)). "A fact is material if its resolution might affect the outcome of the case under the controlling law." Cochran v. Quest Software, Inc., 328 F.3d 1, 6 (1st Cir. 2003) (citation omitted). By invoking summary judgment, "the moving party in effect declares that the evidence is insufficient to support the nonmoving party's case." United States v. One Parcel of Real Prop. (Great Harbor Neck, New Shoreham, R.I.), 960 F.2d 200, 204 (1st Cir. 1992) (citing Celotex Corp. v. Catrett, 477 U.S. 317, 325 (1986)).

"To succeed in showing that there is no genuine dispute of material fact, the moving party must . . . 'affirmatively produce evidence that negates an essential element of the non-moving party's claim,' or, using 'evidentiary materials already on file . . . demonstrate that the non-moving party will be unable to carry its burden of persuasion at trial.'" Ocasio-Hernández v. Fortuño-Burset, 777 F.3d 1, 4–5 (1st Cir. 2015) (quoting Carmona v. Toledo, 215 F.3d 124, 132 (1st Cir. 2000)).

Conversely, "[t]o defeat a properly supported motion for summary judgment, the nonmoving party must establish a trial-worthy issue by presenting enough competent evidence to enable a finding favorable to the nonmoving party." ATC Realty, LLC v. Town of Kingston, N.H., 303 F.3d 91, 94 (1st Cir. 2002) (internal quotations and citation omitted). That is, the nonmoving party must set forth specific, material facts showing that there is a genuine disagreement as to some material fact. One Parcel of Real Prop., 960 F.2d at 204 (citing Anderson., 477 U.S. at 247–48).

In reviewing the record, the Court "must take the evidence in the light most flattering to the party opposing summary judgment, indulging all reasonable inferences in that party's favor." Cochran, 328 F.3d at 6 (citation omitted). The First Circuit has noted that this review "is favorable to the nonmoving party, but it does not give him a free pass to trial." Hannon v. Beard, 645 F.3d 45, 48 (1st Cir. 2011). "The factual conflicts upon which he relies must be both genuine and material[,]" Gomez v. Stop & Shop Supermarket Co., 670 F.3d 395, 397 (1st Cir. 2012), and the Court may discount "conclusory allegations, improbable inferences, and unsupported speculation." Cochran, 328 F.3d at 6 (quoting Medina-Muñoz v. R.J. Reynolds Tobacco Co., 896 F.2d 5, 8 (1st Cir. 1990)).

III. Discussion

A. Judicial Estoppel

Teva contends that Lilly should be precluded from advancing certain factual arguments in the instant proceedings because Lilly took the opposite position in the IPR proceedings and won. [ECF No. 315 at 6]. Those alleged contradictory arguments pertain to the following three fact issues: (1) what a POSA would understand about anti-CGRP antagonist antibodies and the process for preparing them; (2) the techniques available to that POSA to screen anti-CGRP antibodies for antagonistic activity; and (3) the techniques available to that POSA to humanize anti-CGRP antagonist antibodies. [ECF No. 356-1 at 14, 23–25]. Teva asks that the Court hold Lilly to the positions that it took in the IPR proceedings and find that the following facts are established:

1. Anti-CGRP antagonist antibodies were well-known in the art as of 2005;
2. By 2005, a POSA would have considered the techniques for generating anti-CGRP antagonist antibodies "routine" and "conventional";
3. By 2005, the techniques for preparing humanized antibodies from non-human antibodies were well-established and conventional to a POSA;
4. By 2005, conventional humanization techniques that were routinely used preserved the affinity and specificity of the donor antibody.
5. By 2005, assays that measured antagonism, such as cAMP activation assays and radioligand binding assays were conventional and routine means of evaluating whether an anti-CGRP antibody was able to antagonize CGRP.

[ECF No. 315 at 25].

"As a general matter, the doctrine of judicial estoppel prevents a litigant from pressing a claim that is inconsistent with a position taken by that litigant either in a prior legal proceeding or in an earlier phase of the same legal proceeding." InterGen N.V. v. Grina, 344 F.3d 134, 144 (1st Cir. 2003). The purpose of the doctrine is to safeguard the integrity of the courts and avoid

the "perception that either the first or the second court was misled[,]" New Hampshire v. Maine, 532 U.S. 742, 750 (2001), and it applies to a variety of positions a party may take, including an "expression of intention, a statement of fact, or a legal assertion[,]" Alt. Sys. Concepts, Inc. v. Synopsys, Inc., 374 F.3d 23, 34 (1st Cir. 2004) (quoting Wagner v. Prof'l Eng'rs in Cal. Gov't, 354 F.3d 1036, 1044 (9th Cir. 2004)). Judicial estoppel is applied at the court's discretion, but "with caution to avoid impinging on the truth-seeking function of the court." Sexual Minorities Uganda v. Lively, 899 F.3d 24, 32 (1st Cir. 2018) (quoting Perry v. Blum, 629 F.3d 1, 11 (1st Cir. 2010)).

In general, the party seeking to invoke judicial estoppel must satisfy three conditions. Díaz-Báez v. Alicea-Vasallo, 22 F.4th 11, 21 (1st Cir. 2021). First, the prior position of the party to be estopped must be directly inconsistent with its current position such that they are mutually exclusive. Id. It is not enough for the moving party to simply point to an "appearance of inconsistency." Lampi Corp. v. Am. Power Prods., Inc., 228 F.3d 1365, 1377 (Fed. Cir. 2000). Second, the accused party must have persuaded the prior court to accept or otherwise rely on its previous position. Díaz-Báez, 22 F.4th at 21. Third, "the party seeking to assert the inconsistent position must stand to derive an unfair advantage if the new position is accepted by the court." Id. (quoting Knowlton v. Shaw, 704 F.3d 1, 10 (1st Cir. 2013)); see also RFF Family P'ship, LP v. Ross, 814 F.3d 520, 528 (1st Cir. 2016); Alt. Sys., 374 F.3d at 33 (1st Cir. 2004). Courts also "often inquire as to whether judicial acceptance of a party's initial position conferred a benefit on that party." Alt. Sys., 374 F.3d at 33 (citation omitted).

Judicial estoppel is not limited to Article III proceedings, and also applies where a party takes a position in a judicial proceeding that is inconsistent with a position that party took before an administrative tribunal, including in an IPR proceeding before the PTAB. See e.g., Portela-

Gonzalez v. Sec'y of the Navy, 109 F.3d 74, 78 (1st Cir. 1997) ("Equitable doctrines of estoppel apply in administrative and judicial fora."); see also Egenera, Inc. v. Cisco Sys., Inc., 972 F.3d 1367, 1380 (Fed. Cir. 2020) ("[W]e agree that judicial estoppel can occur in an administrative tribunal.")

The Court analyzes in turn each category of Lilly's allegedly inconsistent arguments. To be "clearly inconsistent," positions must be "mutually exclusive" and "directly inconsistent." RFF, 814 F.3d at 528 (quoting Alt. Sys., 374 F.3d at 33).

i. Anti-CGRP Antibodies and the Processes to Make Them

Lilly argued in the Composition of Matter IPRs that murine anti-CGRP antibodies were well-known in the art, [ECF No. 389 ¶ 6], and that "murine monoclonal anti-CGRP antagonist antibod[ies] . . . . were extensively described in the prior art[,]" [id. ¶ 7 (quoting ECF No. 317-2 at 5–6)].[16] Lilly also asserted that "[b]y 2005, several publications had described anti-CGRP antagonist antibodies[,]" [id. ¶ 8 (quoting ECF No. 317-5 at 5)], and that "anti-CGRP antagonist antibodies could be created by known, established, and standard techniques[,]" [id. ¶ 9 (quoting ECF No. 317-5 at 10–11)]. Lilly further claimed that techniques for making murine monoclonal anti-CGRP antagonist antibodies that bind to human CGRP "were extensively described in the prior art[,]" [id. ¶ 11 (quoting ECF No. 317-2 at 5–6)], such that a POSA "would have expected that a similar antibody [*i.e.*, other anti-CGRP antagonist antibodies] could be prepared using

[16] Although Lilly claims to dispute Paragraph 7 of Teva's statement of material facts, after careful consideration of Lilly's response, the Court concludes that there is no factual dispute. Lilly's petition seeking *inter partes* review of one of the Composition of Matter patents states that "The first step in making a humanized anti-CGRP antagonist antibody . . . would have been to make a murine monoclonal anti-CGRP antagonist antibody that binds to human CGRP. Such antibodies, and techniques for making them, were extensively described in the prior art." There can be no good faith dispute that in the latter sentence, Lilly was referring to murine anti-CGRP antagonist antibodies.

routine and conventional antibody preparation methods[,]" [id. ¶ 12 (quoting ECF No. 317-3 at 5)].

In the instant case, Lilly posits that the "state of the art" was "nascent" and "contained minimal information about CGRP antibodies." [ECF No. 389 ¶ 22 (quoting ECF No. 317-1 at 20)].[17] Lilly additionally claims that there were "few reported murine anti-CGRP antibodies" in the prior art and that those that were known "had unpredictable properties and functions, with some *enhancing* CGRP's activity rather than antagonizing it." [Id. ¶ 20 (quoting ECF No. 317-6 at 3)]. Further, with respect to the process for making anti-CGRP antagonist antibodies, Lilly asserts that "[a]s of 2005 and 2006, the art of antibody engineering . . . was highly unpredictable" because "[t]he diversity of antibody repertoire generated by immunizing a live animal, like a mouse, is vast, highly variable, and uncontrollable." [Id. ¶¶ 24–25 (quoting ECF No. 317-1 at 11)].

With the exception of Lilly's contention that the prior art "contained minimal information about CGRP antibodies[,]" [ECF No. 389 ¶ 22 (quoting ECF No. 317-1 at 20)], Lilly's current and prior positions are not so clearly inconsistent as to warrant summary judgment. Lilly's claims in the IPR proceedings that murine anti-CGRP antagonist antibodies were extensively described by multiple publications in the prior art and its argument here, that only a few murine anti-CGRP antibodies had been reported, are not mutually exclusive. The same reasoning applies to Lilly's comments about the processes used to make anti-CGRP antagonist antibodies: that the techniques to make the antibodies were extensively described, such that a POSA could

[17] Lilly also disputes Paragraph 22 of Teva's statement of material facts and argues that Teva's "excerpted and strung together quotations mischaracterize Lilly's disclosures and [its expert's] opinions." [ECF No. 389 ¶ 22]. The Court has closely reviewed the full excerpt offered by Lilly, and does not agree that Teva has misrepresented Lilly's position in the present case.

expect to make other anti-CGRP antagonist antibodies using said techniques, does not foreclose the possibility that the process was also unpredictable and that the outcomes of the process were highly variable.

Conversely, it is exceedingly difficult to square Lilly's argument to the PTAB that murine anti-CGRP antagonist antibodies were well known and extensively described in the prior art with its current argument that the prior art "contained minimal information about CGRP antibodies." [ECF No. 389 ¶ 22 (quoting ECF No. 317-1 at 20)]. As this is a motion for summary judgment, however, the Court must draw all ambiguities and factual inferences in the light most favorable to the non-moving party, Lilly. Lilly's current position is that the prior art contained minimal information about CGRP antibodies, generally, whereas it argued to the PTAB that *anti*-CGRP antibodies, specifically, were well known and extensively described in the prior art. Drawing all inferences in Lilly's favor, as it must, the Court concludes that it's conceivable that while a subset of CGRP antibodies (*i.e.*, anti-CGRP antibodies) was well known, little was known about the larger class of antibodies (*i.e.*, CGRP antibodies, generally). Therefore, the Court concludes that Lilly's positions on this fact issue are not contradictory enough to support summary judgment.

ii. Screening for Antibodies that Antagonize CGRP

In the Composition of Matter IPRs, Lilly argued that by 2005–2006 a POSA had access to routine and conventional assays (*i.e.*, tests) to screen humanized anti-CGRP antibodies to determine whether they possessed desired attributes such as binding to and inhibiting CGRP. [ECF No. 389 ¶ 28]; see e.g., [id. ¶ 29 ("Lilly asserted that 'Teva's own disclosures established that the use of the radioligand binding in SK-N-MC cells is a routine and conventional assay.'") (alteration omitted); id. ¶ 30 ("Lilly asserted that "[a] POSA would . . . have expected to generate

a humanized anti-CGRP antagonist antibody with similar properties that could be evaluated by the well-known and routine radioligand assay in SK-N-MC cells.'"); id. ¶ 33 (Lilly asserted that "as of Teva's earliest filing date, radioligand binding assays in SK-N-MC cells were routinely used for measuring the ability of a CGRP antagonist from [sic] binding of human CGRP with its receptor.")]. Lilly also took the position that "measuring inhibition of cAMP activation [was] a conventional means of evaluating whether an anti-CGRP antagonist antibody is, in fact, an anti-CGRP antagonist."[18] [Id. ¶ 27 (quoting ECF No. 317-4 at 3)]. In addition to asserting that the tests were routine and conventional, Lilly further claimed that "SK-N-MC cells were a commercially available assay medium that a POSA would have had readily available for measuring inhibition of cAMP activation," as "evidenced by [a prior scientific publication]." [Id. ¶ 31 (quoting ECF No. 317-4 at 5)].

Lilly presently argues that the Patents-in-Suit "fail to provide adequate guidance on how to screen for humanized anti-CGRP antagonist antibodies that would be efficacious in treating a human disease." [ECF No. 389 ¶ 41 (quoting ECF No. 317-1 ¶ 285)]. Lilly also avers that the screening process required to practice the claimed methods "would require that same lengthy trial-and-error process for as many as 20^{220} different antibody sequences . . . ." [Id. ¶ 42 (quoting ECF No. 317-1 ¶ 278)]. Further, Lilly claims that "conducting cAMP and in vivo animal assays to adequately characterize a single compound requires significant work and time for setting up the experimentation, selecting and evaluating appropriate controls, testing the compound of interest itself, and appropriately evaluating the results . . . . Overall, conducting such assays for

[18] Lilly claims to dispute that it took this position in the IPRs, asserting that its petition merely cited to Teva's patent's admissions, not the prior art. [ECF No. 389 ¶ 27]. Having reviewed Lilly's petition for *inter partes* review, it is clear that, whether or not Lilly was citing Teva's patent's admissions, it was adopting the position that measuring the inhibition of cAMP activation was a conventional means of evaluating CGRP antagonism.

even a single compound would take at least four months." [Id. ¶ 43 (quoting ECF No. 317-6 ¶ 329)].

Here, again, Lilly's positions are not so contradictory as to warrant summary judgment. In the IPR proceedings, Lilly argued that tests used to screen antibodies for desired traits were conventional, routine, and commercially available. Lilly did not argue, importantly, that tests that identified whether, for example, an antibody binds to CGRP, also indicate whether the test will be efficacious in treating human disease such as migraine. Further, Lilly's position before the PTAB that a test was routine is not inconsistent with its present argument that the screening process to identify antibodies covered by the claimed methods would be lengthy and require significant time and effort. Because Lilly's positions are not more specifically contradictory, the Court will not impose the harsh sanction of judicially estopping Lilly from making arguments in the instant action that merely differ from positions asserted in prior proceedings, although the Court will, where appropriate, allow cross examination on this topic.

iii. Humanizing murine anti-CGRP antagonist antibodies

In the IPRs, Lilly argued that the process of humanizing non-human (*e.g.*, murine) antibodies "was a well-established and routine procedure by 2005." [ECF No. 389 ¶ 44 (quoting ECF No. 317-5 at 3)]. Lilly also discussed a prior art reference, Queen, U.S. Pat. No. 6,180,370, issued Jan. 30, 2001, and observed that it "describes routine and conventional humanization technologies that have been recognized as the 'gold standard' years before 2005." [Id. ¶ 45 (quoting ECF No. 317-5 at 10)]; see also [id. ¶ 47 (quoting ECF No. 315-5 at 18) (Lilly asserting that Queen "discloses well-established prior art techniques to generate humanized antibodies for therapeutic use that maintained the original binding attributes of the donor non-human antibodies.")]. Lilly further argued that, relying on Queen's "routine humanization process," a

POSA "would have readily been able to" humanize an antibody "while maintaining or even improving the binding specificity and affinity for human CGRP." [Id. ¶ 46 (quoting ECF No. 317-2 at 7)].

Lilly now argues that in 2005–2006, the methods for humanization "were both laborious and fraught with unpredictability" and it "was an empirical, unpredictable, time-consuming, and expensive process, taking anywhere from four months to a full year, requiring multiple full-time employees, and costing about $500,000 for each humanized antibody." [ECF No. 389 ¶¶ 55 (quoting ECF No. 317-6 ¶ 331), 60 (quoting ECF No. 317-10 ¶ 50)]. Lilly additionally alleges that humanization was a "trial and error exercise," required "experimentation," with "no guarantee of success at the end," and that the process "typically reduced or eliminated the ability of the antibody to bind to its target[.]" [Id. ¶¶ 56–57 (quoting ECF No. 317-1 ¶¶ 62, 270, 288–89)].

Here, again, Lilly's arguments regarding humanization techniques, while different from the points advanced during the IPR proceedings, are not so different as to be considered mutually exclusive. A process may be routine and conventional while also being unpredictable, costly, and burdensome. The former does not preclude the latter and therefore the sanction of judicial estoppel is not warranted.

Having concluded that Lilly's arguments to this Court are not so obviously inconsistent as to warrant summary judgment, it is not necessary to further consider whether Lilly persuaded the PTAB to adopt its prior arguments or whether Lilly would derive an unfair advantage if this Court accepted its new position. The Court similarly need not consider Lilly's argument that Teva's motion failed to comply with Fed. R. Civ. P. 56(a) because it did not seek judgment on any claim or defense.

B. Inequitable Conduct and Unclean Hands

Lilly asserts that the Patents-in-Suit are unenforceable because (1) during prosecution before the PTO, Teva intentionally withheld material prior art references and data from certain preliminary experiments, and (2) with respect to the '907 and '908 patents, because doctors involved in patent prosecution on Teva's behalf intentionally delayed filing paperwork that was necessary to correct otherwise defective patent applications and falsely averred that the delay was unintentional. [ECF No. 302 at 6–7]. Teva moves for summary judgment on these defenses, contending that Lilly cannot shoulder the heavy evidentiary burden of proving inequitable conduct. [Id. at 11, 23–24].

The burden of proof is significant. "Inequitable conduct is an equitable defense to patent infringement that, if proved, bars enforcement of a patent." Therasense, Inc. v. Becton, Dickinson & Co., 649 F.3d 1276, 1285 (Fed. Cir. 2011) (en banc). "The remedy for inequitable conduct is [known as] the 'atomic bomb' of patent law," because "inequitable conduct as to any individual claim renders the entire patent unenforceable." Id. at 1288.

Inequitable conduct has two requirements: materiality and intent. Therasense, 649 F.3d at 1290. "[T]he materiality required to establish inequitable conduct is but-for materiality[,]" id. at 1291, for present purposes "meaning that 'the PTO would not have allowed a claim had it been aware of the undisclosed prior art[,]'" TransWeb, LLC v. 3M Innovative Properties Co., 812 F.3d 1295, 1304 (Fed. Cir. 2016) (quoting Therasense, 649 F.3d at 1291–92).

To show intent, "the accused infringer must prove that the patentee acted with the specific intent to deceive the PTO." Therasense, 649 F.3d at 1290. In cases involving nondisclosure of information, as alleged here, "the accused infringer must prove by clear and convincing evidence that the applicant knew of the undisclosed information, knew it was

material, and made a deliberate decision to withhold it." Id. In other words, "[p]roving that the applicant knew of a reference, should have known of its materiality, and decided not to submit it to the PTO does not prove specific intent to deceive." Id. Courts may infer intent from indirect and circumstantial evidence, however, "to meet the clear and convincing evidence standard, the specific intent to deceive must be 'the single most reasonable inference able to be drawn from the evidence.'" Id. (quoting Star Sci., Inc. v. R.J. Reynolds Tobacco Co., 537 F.3d 1357, 1366 (Fed. Cir. 2008)).

Here, Lilly contends that Teva, and specifically Drs. Zeller and Pons, engaged in inequitable conduct by intentionally omitting (1) a prior art reference, Shaw, (2) the results of internal data from failed attempts to identify anti-CGRP antagonist antibodies that bound to the N-terminal end or mid-region of CGRP, and (3) data from a cortical spreading depression ("CSD") assay. [ECF No. 302 at 7].

i. Shaw

Shaw is a prior art reference that includes data on an antibody that bound to the mid-region of CGRP but failed to antagonize it, [ECF No. 387 ¶¶ 32, 68], and, among other things, discussed antibodies that bound to the N-terminal end of CGRP, one of which antagonized CGRP, and others that did not, [id. ¶ 33]. Prior to submitting applications for any of the Patents-in-Suit, Dr. Zeller summarized Shaw's findings, with respect to antibodies that bind to the mid-region of CGRP, to other named inventors. See [ECF No. 387 ¶ 13]. Lilly alleges that Teva acted inequitably by failing to disclose Shaw in the '045 application and by burying it in the '907 and '908 applications among 400 other references without discussing its significance. [ECF No. 348 at 10].

According to Lilly, Shaw is material, and not cumulative, because it teaches that some antibodies that bind to the N-terminal end and mid-region do not antagonize CGRP. [ECF No. 348 at 22]. This teaching, in Lilly's view, undermines Teva's argument to the PTO during prosecution that because the antibodies in the Patents-in-Suit bind to the C-terminal end of CGRP—the epitope furthest from the region responsible for activating CGRP—"any antibody that effectively binds CGRP may reasonably be expected to have the claimed effect," *i.e.*, antagonize CGRP. [ECF No. 387 ¶ 64 (quoting ECF No. 354-14 at 11)]. Lilly contends that if Shaw had been disclosed, the patent examiner would have rejected Teva's argument and the '045 patent would not have issued because Shaw identifies antibodies that bind to epitopes other than the C-terminal and do not in fact antagonize CGRP. See [id. ¶¶ 25–27 (Lilly citing to Dr. McDonnell's opening and reply reports)]. Lilly also argues that even though Shaw was disclosed in the '907 and '908 patents, it was buried and Teva did nothing to highlight it despite its significance and tendency to contradict Teva's prior assertion. [Id. ¶¶ 25, 29, 51]. Given Shaw's alleged significance, Teva's failure to disclose it in the '045 application and its decision to bury it in the '907 and '908 applications, Lilly contends that a reasonable juror could conclude that the most reasonable inference is that Teva withheld it with the intent to deceive the PTO. [ECF No. 348 at 20–22].

Teva responds that Shaw was cumulative and not material because the patent, and a prior publication—Tan et al., *Demonstration of the neurotransmitter role of calcitonin gene-related peptides (CGRP) by immunoblockade with anti-CGRP monoclonal antibodies*, 111 Br. J. Pharmacol. 703–10 (1994) ("Tan 1994")—already disclosed certain antibodies that bind to CGRP but do not antagonize it. [ECF No. 302 at 15]. Therefore, according to Teva, Shaw's

teaching—that antibodies that bind to the mid-region and N-terminal of CGRP may not antagonize it—was unlikely to change the patent examiner's view of patentability. [Id.].

The Court finds that there is a genuine dispute about Shaw's materiality. While Teva argues that Shaw was cumulative because the patent specification and Tan 1994 also teach that antibodies that bind to CGRP may not antagonize it, that argument overlooks the fact that Shaw specifically and additionally teaches that antibodies that bind to the N-terminal and mid-region may fail to antagonize CGRP. See [ECF No. 387 ¶¶ 37–38]. That additional disclosure undermines Teva's argument that Shaw is merely cumulative of information disclosed in the patent specification. Drawing all inferences in favor of the non-moving party, the Court further finds that a reasonable juror could conclude that if Shaw had been disclosed the patent examiner would have rejected Teva's claim that antibodies that bind to regions other than the C-terminal (*e.g.*, the mid-region or N-terminal) can be reasonably expected to antagonize CGRP, and, in turn, not allow the patent to issue.

As to intent, Teva argues there is no direct evidence that Drs. Zeller or Pons considered disclosing Shaw to the PTO and deliberately chose to withhold it and that there are other reasonable inferences the jury could reach. [ECF No. 302 at 21]. To begin, the question is not whether there are simply other reasonable inferences, as Teva appears to suggest in its motion, see [id. at 19–21], rather, at summary judgment, the question is if there is a genuine dispute regarding whether a reasonable factfinder could conclude that the most reasonable inference is that Shaw was withheld with the intent to deceive the PTO. Therasense, 649 F.3d at 1290. Having closely considered the record, the Court cannot conclude that a reasonable juror could not find that the most reasonable inference is that Drs. Zeller and Pons sought to deceive the PTO by withholding Shaw in the '045 application and not highlighting it in the '907 and '908

applications. The Court thus finds that these are factual matters best left to the factfinder and summary judgment is denied.

ii. Internal Binding Data & CSD Assay Data

Lilly next claims that Teva, and Drs. Zeller and Pons, engaged in inequitable conduct by withholding the results of internal data from failed attempts to identify anti-CGRP antagonist antibodies that bound to the N-terminal end or mid-region of CGRP ("Binding Data"). See [ECF No. 387 ¶ 14]. In Lilly's view, the Binding Data is material because it shows that Teva did not possess the full scope of the claimed methods. [ECF No. 348 at 20]. For that reason, Lilly suggests that Drs. Zeller and Pons were incentivized to withhold the data as disclosing it would have potentially prevented Teva from securing a broad patent. [Id. at 15–16].

Lilly also alleges that during prosecution of the Patents-in-Suit, Teva, and specifically Drs. Zeller and Pons, withheld the results of a CSD assay that showed that an anti-CGRP antagonist antibody did not inhibit a signal related to migraine.[19] [ECF No. 387 ¶ 55]. Lilly claims that Dr. Pons was on notice of the importance of the test because he was on an email chain in which another scientist stated that if the anti-CGRP antibody "doesn't work" in the assay, "then the whole concept in questionable." [Id. ¶ 57 (quoting ECF No. 354-26 at 2) (email from Robert Klein to, among others, Dr. Pons)]. Dr. Zeller was similarly on notice of the CSD assay's relevance, says Lilly, because he stated that the data from the study would "be crucial in identifying whether or not the peptide is an effective therapeutic for migraine." [Id. ¶ 54 (quoting ECF No. 364-21 at 3)]. In light of the alleged importance of the test, Lilly argues (1) that if the results had been disclosed, the PTO would not have allowed the patent to issue based

[19] In addition to disputing whether the results of the CSD assay were material, the parties also dispute whether the test results were negative or merely inconclusive. See [ECF No. 348 at 17].

on lack of utility and possession, [id. ¶ 56], and (2) that a factfinder could conclude that the most reasonable inference is that the results were withheld with the intent to deceive the PTO, [ECF No. 348 at 23–24].

In response, Teva argues that Lilly has not pointed to any evidence to suggest that the Binding Data or the CSD assay results are material or, in other words, would have led the PTO to reject any claims of the Patents-in-Suit. [ECF No. 302 at 13, 16]. Teva notes that Lilly's own expert, Dr. McDonnell, testified that when he described the Binding Data as material, he meant only that it "could have been relevant for [the PTO's patentability] assessment," [ECF No. 387 ¶ 25 (quoting ECF No. 354-7 at 151:5–10); ECF No. 302 at 13], and, with respect to the CSD assay, another of Lilly's experts described the results as merely "germane to the patent issue[.]" [ECF No. 387 ¶ 28 (quoting ECF No. 304-18 at 214:3–8)]. Teva further argues that the CSD assay is not material because the results were not dispositive in determining whether an anti-CGRP antibody can treat migraine or other head pain. [ECF No. 302 at 16].

As for intent, Teva asserts that no reasonable factfinder could exclude the possibility that Drs. Zeller and Pons did not consider disclosing the results of the internal testing or the results of the CSD assay to the PTO because they did not make final decisions about what information to disclose or that they did not view it as particularly relevant because, for example, they thought it was inconclusive. [ECF No. 302 at 20–23; ECF No. 387 ¶ 57].

The Court again finds that there are genuine disputes with respect to materiality and intent that preclude summary judgment. Drawing all inferences in favor of Lilly, a reasonable factfinder could conclude that disclosure of the Binding Data, which revealed that Teva's scientists had been unable to identify an anti-CGRP antagonist antibody that bound to a region other than the C-terminal, may have caused the PTO to refrain from issuing the broad Patents-in-

Suit. A similar inference is reasonable with respect to the results of the CSD assay, which could be interpreted to suggest that the claimed invention was inoperative, and thus cause the examiner to reject the application. Based on the potential negative impacts of disclosing the data, the Court further finds that a reasonable factfinder could conclude that the most reasonable inference is that the data and results were withheld with the intent to deceive the PTO.

iii. Petitions for Unintentional Delay

Lilly next argues that Teva is liable for inequitable conduct committed by patent agent Adam Cole and patent attorney Jeffery Giering during prosecution of the patent applications that led to the '907 and '908 patents. [ECF No. 348 at 12]. In particular, Lilly claims that Cole and Giering intentionally delayed filing petitions to correct three patent applications that had initially claimed priority to an abandoned application (the '394 application). [Id.]. The intentional delay can be inferred, according to Lilly, from the fact that, after receiving notice that the '394 application had been abandoned, Cole and Giering waited more than a year to file the first petition to correct the '871 application. [Id. at 13]. They then waited an additional five months to file identical corrections in two other pending applications (the '816 and '925 applications). [Id. at 24; ECF No. 387 ¶ 85]. Lilly asserts that because Cole and Giering were on notice of the errors in all three applications at least as early as the date they filed the motion for the first petition, it is not conceivable that the entire period of delay was unintentional. [ECF No. 348 at 24; ECF No. 387 ¶¶ 85, 87]. Lilly thus argues that Cole and Giering's attestation that the delay was unintentional, at least as to the second and third petitions, was false and evidences an intent to deceive the PTO to hide their error and save the patents. [ECF No. 348 at 24]. The submission, and later approval, of the petitions was material to the issuance of the '907 and '908

patents, in Lilly's view, because the patents would have been considered invalid and would not have issued. [Id.].

Teva does not contest that the petitions were material but argues that intent to deceive is not the most reasonable inference because there is no evidence that the delay was intentional or that Cole and Giering knew the statements were wrong and made them with the intent to deceive. [ECF No. 302 at 24].

Here, again, the Court finds that there is a genuine dispute of fact as to intent such that summary judgment is not warranted. Teva appears to argue, in part, that the Court should grant summary judgment because there is no direct evidence that the delay was intentional. However, "a district court may infer intent from indirect and circumstantial evidence." Therasense, 649 F.3d at 1290 (citation omitted). Lilly has presented circumstantial evidence that the representations in the second and third petitions were false and also proffered an explanation as to why Drs. Cole and Giering would have been motivated to deceive the PTO. A factfinder could thus conclude that the most reasonable inference is that Drs. Cole and Giering made a false representation to the PTO with the intent to deceive. Therefore, the Court declines to grant summary judgment on this issue.

C. Willful Infringement

Lilly requests the Court enter summary judgment against Teva on its claim for willful infringement, arguing that even if Lilly infringed—which it denies—there is no evidence it did so willfully. [ECF No. 306 at 5–6]. Under 35 U.S.C. § 284, a district court may enhance damages for patent infringement up to three times the amount found or assessed. The awarding of enhanced damages, however, is "generally reserved for egregious cases of culpable behavior." Halo Elecs., Inc. v. Pulse Elecs., Inc., 579 U.S. 93, 104 (2016); see also Crane Sec. Techs., Inc.

v. Rolling Optics AB, 337 F. Supp. 3d 48, 57 (D. Mass. 2018). Indeed, "[t]he sort of conduct warranting enhanced damages has been variously described . . . as willful, wanton, malicious, bad-faith, deliberate, consciously wrongful, flagrant, or—indeed—characteristic of a pirate." Id. at 103–04.

Willfulness requires "specific intent to infringe at the time of the challenged conduct." Bayer Healthcare LLC v. Baxalta Inc., 989 F.3d 964, 987 (Fed. Cir. 2021) (citing Halo, 579 U.S. at 105–06). Therefore, "[k]nowledge of the asserted patent and evidence of infringement is necessary, but not sufficient, for a finding of willfulness." Bayer, 989 F.3d at 988. Instead, a determination of willfulness also requires a finding of "deliberate or intentional" infringement. See SRI Int'l, Inc. v. Cisco Sys., Inc., 14 F.4th 1323, 1330 (Fed. Cir. 2021) (quoting Eko Brands, LLC v. Adrian Rivera Maynez Enterps., Inc., 946 F.3d 1367, 1378 (Fed. Cir. 2020)). Whether the infringement was deliberate or intentional must be determined, based on all the circumstances, by the factfinder. See WCM Indus., Inc. v. IPS Corp., 721 F. App'x 959, 970 (Fed. Cir. 2018) (quoting Gustafson, Inc. v. Intersystems Indus. Prods., Inc., 897 F.2d 508, 510–11 (Fed. Cir. 1990)). "[A] patentee need only establish willfulness by a preponderance of the evidence . . . ." SiOnyx, LLC v. Hamamatsu Photonics K.K., 330 F. Supp. 3d 574, 609 (D. Mass. 2018) (citation omitted).

There is no dispute that Lilly had knowledge of the Patents-in-Suit prior to the date of the first alleged infringement. See [ECF No. 395 ¶ 105 ("In a September 27, 2021 email, Lilly agreed to stipulate that 'Lilly possessed knowledge of [the '045 patent] as of October 24, 2017' and that 'Lilly possessed knowledge of [the '907 and '908 patents] as of February 6, 2018.") (quoting ECF No. 308-72 at 2, 7)]. Therefore, the Court need only determine whether there is a genuine dispute as to whether Lilly, if it infringed at all, did so willfully.

When determining whether alleged infringement was willful, courts look to evidence of the accused infringer's intent "at the time of the challenged conduct" based on the totality of the circumstances. See Bayer, 989 F.3d at 987; BASF Plant Science, LP v. Commonwealth Sci. and Indus. Rsch. Org., 28 F.4th 1247, 1274 (Fed. Cir. 2022) (citation omitted). Here, the alleged infringing conduct—Lilly's sale of Emgailty—began in October 2018. [ECF No. 395 ¶ 94]. Lilly argues that summary judgment is warranted because there is no evidence, as of October 2018, that Lilly intentionally or deliberately infringed Teva's patents, [ECF No. 306 at 6], and because Lilly's reasonable belief of noninfringement is evidenced by its immediate filing of petitions for IPR. [ECF No. 395 ¶ 3–4]. Even excluding all evidence related to actions that Lilly took after the first alleged infringement, the Court finds that there are genuine disputes of fact that preclude summary judgment. To begin, the parties dispute whether Lilly, in its development of Emgality, copied the Patents-in-Suit, which would be "strong evidence of willful infringement . . . ." L.A. Gear, Inc. v. Thom McAn Shoe Co., 988 F.2d 1117, 1127 (Fed. Cir. 1993); KAIST IP US LLC v. Samsung Elecs. Co., 439 F. Supp. 3d 860, 884–85 (E.D. Tex. 2020), appeal dismissed sub nom. KIPB LLC v. Samsung Elecs. Co., Ltd., 2020-1619, 2020 WL 9175080 (Fed. Cir. Sept. 3, 2020) (upholding a jury's willfulness finding based, in part, on the accused infringer copying the patented technology). Moreover, Lilly admits that it had knowledge of the Patents-in-Suit at the time of infringement yet, leading up to October 2018, began an expensive marketing campaign to promote and sell its allegedly infringing product. Lilly urges the Court to disregard that evidence and accept its claim that it always believed the Patents-in-Suit were invalid or otherwise unenforceable and thus, at a minimum, did not infringe willfully, if at all. A determination of Lilly's subjective belief, however, turns on a review of the totality of the evidence, including the credibility of witnesses and the weight to be given to certain evidence,

which is properly left to the jury. The Court therefore will not grant summary judgment on the issue of willful infringement.

D. Non-Infringement

Lilly moves the Court to find that Lilly's Galcanezumab (*i.e.*, Emgality) does not infringe claims 18 and 21 of Teva's '045 patent. [ECF No. 298 at 6]. Of the 20 claims that Teva claims Lilly has infringed, claims 18 and 21 are the only claims that set forth specific amino acid sequences for, respectively, the CDRs and variable regions, as shown below:

> 18. The method according to claim 17,[20] wherein the anti-CGRP antagonist antibody is:
>
> (a) an antibody having a CDR H1[21] as set forth in SEQ ID NO: 3; a CDR H2 as set forth in SEQ ID NO: 4; a CDR H3 as set forth in SEQ ID NO:5; a CDR L1 as set forth in SEQ ID NO: 6; a CDR L2 as set forth in SEQ ID NO: 7; and a CDR L3 as set forth in SEQ ID NO: 8; or
>
> (b) a variant of an antibody according to (a) as shown in Table 6.[22]
>
> * * *
>
> 21. The method according to claim 17, wherein the anti-CGRP antagonist antibody comprises a V_H[23] domain comprising SEQ ID NO: 1 and V_L domain comprising SEQ ID NO: 2.

[ECF No. 406 ¶¶ 43, 47]. Therefore, claim 18 recites the use of an anti-CGRP antagonist antibody that either has the same sequence in its CDRs as either Antibody G1 or one of

[20] Claim 17 recites: "A method for reducing incidence of or treating headache in a human, comprising administering to the human an effective amount of an anti-CGRP antagonist antibody, wherein said anti-CGRP antagonist antibody is a human monoclonal antibody or a humanized monoclonal antibody. [ECF No. 406 ¶ 41].

[21] The designations "H1," "H2," and "H3" refer to the first, second and third CDRs located on the heavy chain. [ECF No. 406 ¶ 44]. The designations "L1," "L2," and "L3" refer to the first, second and third CDRs located on the light chain. [Id. ¶ 45].

[22] Table 6 refers to the amino acid sequences of the 84 variants of Antibody G1 that are listed in Table 6 of the '045 patent. [ECF No. 406 ¶ 66].

[23] V_H refers to the variable domain of the heavy chain and V_L refers to the variable domain of the light chain.

the variants of Antibody G1 that are listed in Table 6 of the '045 patent. [Id. ¶¶ 43, 46]. Claim 21, in turn, recites the use of antibodies that have variable domains with amino acid sequences identical to those of Antibody G1. See [id. ¶ 48].

Lilly's antibody, Galcanezumab, has amino acid sequences in its CDRs and variable regions that differ from Antibody G1 or any of the variants listed in Table 6 of the '045 patent. [ECF No. 406 ¶ 130]. For example, the amino acid sequences of Galcanezumab's CDRs have 29.9% sequence identity (*i.e.*, similarity) with Antibody G1. [Id. ¶ 132]. Additionally, the heavy and light chain variable domains of Galcanezumab and Antibody G1 have 50.8% and 64.5% sequence identities, respectively. [Id. ¶ 135]. As for the variants, Antibody M2 is the variant with the most similar heavy chain variable domain as compared to Galcanezumab, but its amino acid sequence has only 52.5% similarity. [Id. ¶ 136].

In addition to having distinct amino acid sequences in its CDRs and variable regions, Galcanezumab has functional differences from Antibody G1. [ECF No. 406 ¶¶ 147–50]. Galcanezumab, for instance, binds to the mid-region of CGRP, whereas Antibody G1 binds to the C-terminal end. [Id. ¶¶ 147–48].[24] Further, and among other functional differences, Galcanezumab binds to CGRP five-times more rapidly than Antibody G1. [Id. ¶ 165].

"The patentee has the burden of proving infringement by a preponderance of the evidence." Amgen Inc. v. Sandoz Inc., 923 F.3d 1023, 1027 (Fed. Cir. 2019). "To establish literal infringement, every limitation set forth in a claim must be found in an

[24] Lilly claims that all of the antibodies disclosed in the Patents-in-Suit bind to the C-terminal end of CGRP, but Teva disputes this. [ECF No. 406 ¶ 149].

accused product, exactly." Duncan Parking Techs., Inc. v. IPS Grp., Inc., 914 F.3d 1347, 1360 (Fed. Cir. 2019) (internal quotation marks and citation omitted). "[A] product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 21 (1997) (citing Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 609 (1950)).

The Supreme Court has created two frameworks for evaluating equivalence: the function-way-result test ("FWR") (whether the accused product performs substantially the same function in the same way to obtain the same result) and the insubstantial differences test (whether the accused product is substantially different from what is patented). Mylan Institutional LLC v. Aurobindo Pharma Ltd., 857 F.3d 858, 866–67 (Fed. Cir. 2017) (citing Graver Tank, 339 U.S. at 608, 609). The Supreme Court has acknowledged that the suitability of the two tests may vary, depending on the circumstances of the case, and the Federal Circuit has further advised that the FWR test "may be less appropriate for evaluating equivalence in chemical compounds" because it can fail to "capture substantial differences between a claimed and accused compound." Id. at 869.

Under either framework, the doctrine of equivalence is limited by the "all elements rule," which holds that "an accused product or process is not infringing unless it contains each limitation of the claim, either literally or by an equivalent." Freedman Seating Co. v. Am. Seating Co., 420 F.3d 1350, 1358 (Fed. Cir. 2005). In other words, the doctrine of equivalence may not be applied in such a way as to "effectively eliminate"

or "vitiate" any claim element. Warner-Jenkinson, 520 U.S. at 29–30. Vitiation, however, "is not an exception to the doctrine of equivalents, but instead a legal determination that 'the evidence is such that no reasonable jury could determine two elements to be equivalent.'" Deere & Co. v. Bush Hog, LLC, 703 F.3d 1349, 1356 (Fed. Cir. 2012) (quoting Warner-Jenkinson, 520 U.S. at 39 n.8).

Lilly argues that Teva's equivalence theory, with respect to claims 18 and 21 of the '045 patent, is overbroad and impermissibly vitiates multiple claim limitations. [ECF No. 298 at 7]. In Lilly's view, claims 18 and 21 are limited by specific amino acid sequences and Teva's product, Galcanezumab, has substantially different sequences. [Id. at 13]. In addition to differences in the specific amino acid sequence, those differences cause Galcanezumab to have different functional properties than Lilly's product, Fremanezumab. Lily asserts that these functional differences as well as the differences in amino acid sequence, place Galcanezumab far beyond any permissible scope of equivalents. [Id. at 15–16]. Lilly also argues that the Court should apply the insubstantial differences framework when analyzing equivalence instead of the FWR test. [Id. at 17]

Teva's main argument in response to Lilly's motion is that there is a genuine dispute as to whether Lilly's Galcanezumab infringes claims 18 and 21 of the '045 patent. [ECF No. 360 at 6]. While Teva concedes that Galcanezumab's amino acid sequences are not identical to the limitations in claims 18 and 21, and therefore does not literally infringe, it argues that Galcanezumab is equivalent because the differences in amino acid sequence do not translate into meaningful real-world biological differences when the antibodies are deployed to treat headache patients. [Id.]. Teva avers that the

corresponding sequences: "(i) perform substantially the same biochemical function by binding to CGRP such that CGRP is blocked from engaging with its receptor; (ii) do this in substantially the same way by binding to the particular regions of CGRP required for receptor engagement with high affinity, selectivity, and duration; and (iii) achieve substantially the same result—the treatment of headache symptoms in patients due to a reduction in CGRP signaling." [Id.]

Teva further claims that there are additional genuine disputes that preclude summary judgment, including that the parties disagree about: (1) the proper scientific framework used to perform the FWR test, [ECF No. 360 at 8 (citing Crown Packaging Tech., Inc. v. Rexam Beverage Can Co., 559 F.3d 1308, 1315 (Fed Cir. 2009))]; (2) the meaning and significance of clinical and pre-clinical data, [id. at 11–12]; (3) the substance and impact of the research of the named inventors of the '045 patent, [id. at 12–13]; and (4) whether Lilly independently developed Galcanezumab or relied on Teva's patents to do so, [id.].

In addition to there being disputed material facts, Teva argues that summary judgment should be denied because Lilly's statement of facts violates the Federal Rules of Civil Procedure and Local Rules of the District of Massachusetts, and because Lilly's argument that Teva's theory of equivalences conflicts with the equitable rationale underlying the doctrine of equivalents fails. [ECF No. 360 at 15–16].

As the parties agree that Galcanezumab's amino acid sequences are, at minimum, nominally different from the limitations of claims 18 and 21 of the '045 patent, there is no dispute that the accused product does not literally infringe the patents claims. Thus the Court need only determine whether there is a genuine dispute as to whether

Galcanezumab infringes claims 18 and 21 of the '045 patent under the doctrine of equivalents. As discussed above, the Supreme Court has "blessed two equivalent tests"—the FWR and insubstantial differences tests—and "le[ft] to the lower courts in future cases the choice of which to apply." Mylan, 857 F.3d at 867. In deciding which test to use, the Court considers the observations by the Supreme Court and Federal Circuit that "non-mechanical cases may not be well suited to consideration under the FWR test" and that is "particularly true in the chemical arts."[25] Id. With respect to the claims at issue, which recite specific amino acid sequences (*i.e.*, specific structures), the Court finds that the FWR test is poorly suited for the equivalence analysis and elects to apply the insubstantial differences test.

Teva's primary argument is that even though Galcanezumab's amino acid sequences differ, it is nonetheless equivalent because it achieves the same result—binding to CGRP with sufficient strength to reduce CGRP signaling—and also because it has six CDRs and two variable domains as required by claims 18 and 21. See [ECF No. 360 at 18–19]. In Teva's view, the key inquiry is not whether the amino acid sequences are different, but whether the differences matter in the claimed method—*i.e.*, treating headache. [Id. at 19]. Teva's argument is a bridge too far. Claims 18 and 21 of the '045 patent recite specific amino acid sequences for the CDRs and variable domains, respectively, which reflects that Teva chose to limit these claims to require these specific

[25] The shortcomings of the FWR test in the context of pharmaceutical treatments is exemplified by the comparison of aspirin and ibuprofen. Persons of skill in the art would not consider these two medications to have structural equivalents under the insubstantial differences test. If you analyze them under the FWR test, however, they would appear to be equivalents because they "each provide analgesia and anti-inflammatory activity ('function') by inhibiting prostaglandin synthesis ('way') in order to alleviate pain, reduce fevers, and lessen inflammation ('result')." Mylan, 857 F.3d at 869.

sequences despite the fact that "claim[s] that contain[] [] detailed recitation of structure [are] properly accorded correspondingly limited recourse to the doctrine of equivalents." Bicon, Inc. v. Straumann Co., 441 F.3d 945, 955 (Fed. Cir. 2006) (citation omitted). Here, "by defining the claim in a way that clearly excluded certain subject matter, the patent implicitly disclaimed the subject matter that was excluded and thereby barred the patentee from asserting infringement under the doctrine of equivalents." Id. (quoting SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1346 (Fed. Cir. 2001)).

Because Lilly's antibody, Galcanezumab has CDRs and variable regions with amino acid sequences that are substantially different from Antibody G1 or any of its variants, the amino acid sequences in Galcanezumab are clearly excluded from the amino acid sequences recited by claims 18 and 21. Moreover, Teva's equivalence argument would read the amino acid sequence limitation out of claims 18 and 21 and effectively expand the scope of that limitation to encompass any amino acid sequence in a full-length antibody that has the effect of sufficiently antagonizing CGRP. As discussed, however, claims 18 and 21 list the amino acid sequences of the CDRs and variable domains of Antibody G1 and its variants, not the antibody sequences of Galcanezumab. Accordingly, the Court finds that Galcanezumab does not infringe claims 18 or 21 under the doctrine of equivalents.

The Court also disagrees with Teva that summary judgment is inappropriate based on the parties' disputes over clinical and pre-clinical data, the substance and impact of the research of the named inventors of the '045 patent, and whether Lilly relied on the Patents-in-Suit to develop Galcanezumab. These issues, even if disputed, do not bear on

whether Galcanezumab infringes claims 18 and 21 under the doctrine of equivalents and therefore are not material. The Court further declines Teva's invitation to deny summary judgment based on Lilly's statement of fact. Together the parties have filed far in excess of 1,000 pages of claimed statements of facts that improperly contain legal arguments and disputed facts with the result being a time-consuming process to identify the much smaller subset of facts that are actually undisputed. Where both parties have engaged in the same malfeasance, the Court will not reward one and punish the other. Therefore the Court grants Lilly's motion for partial summary judgment of non-infringement with respect to claims 18 and 21 of the '045 patent.

E. Written Description

Lilly claims that all of Teva's asserted claims from the '045, '907, and '908 patents are invalid because they do not satisfy 35 U.S.C. § 112's written description requirement and seeks summary judgment on this dispositive issue. [ECF No. 294-1 at 7]. Section 112 states that a patent specification "shall contain a written description of the invention." 35 U.S.C. § 112. "[T]he hallmark of written description is disclosure," and the test is "an objective inquiry into the four corners of the specification from the perspective of a [POSA]." Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "A specification adequately describes an invention when it 'reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.'" Juno Therapeutics, Inc. v. Kite Pharma, Inc., 10 F.4th 1330, 1335 (Fed. Cir. 2021) (quoting Ariad, 598 F.3d at 1351). Context matters, however, and "[w]hat is required to meet the written description requirement 'varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.'" Juno, 10 F.4th at 1335 (quoting Capon v. Eshhar, 418 F.3d

1349, 1357 (Fed. Cir. 2005)). "Whether a patent claim is supported by an adequate written description is a question of fact . . . ." AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285, 1297 (Fed. Cir. 2014).

The Federal Circuit has set forth a number of factors to consider when evaluating the adequacy of disclosure for generic claims, including "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, and the predictability of the aspect at issue." Id. at 1299 (internal quotation marks and citation omitted). "For genus claims using functional language, . . . the written description 'must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus." Juno, 10 F.4th at 1335 (quoting Ariad, 598 F.3d at 1349). "Where representative [species] are necessary to satisfy the written description requirement, the number of such [species] that must be disclosed depends on the context, including the knowledge already available in the art." Erfindergemeinschaft UroPep GbR v. Eli Lilly and Co., 276 F. Supp. 3d 629, 650 (E.D. Tex. 2017); see also Ariad, 598 F.3d at 1351 ("[No] bright-line rules govern[] . . . the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in a field."). In deciding this issue, the Court looks to the specification as it would be viewed by a POSA, which, in effect, incorporates the knowledge in the prior art and, as it must, draws all inferences in favor of Teva, the non-moving party.

i. Disclosure of Claimed Antibodies

Lilly first argues that Teva's specifications do not provide a sufficient number and variety of humanized or human anti-CGRP antagonist antibodies to show possession of its functionally

defined genus, which, Lilly says, is necessary for an adequate written description. Lilly asserts that "the need [for Teva] to adequately describe the claimed antibodies is particularly acute because the patents claim the use of an entirely new genus of compounds." [ECF No. 399 at 11]. Teva responds that Lilly has framed the inquiry incorrectly because Teva is only claiming a new method for using certain antibodies to treat headaches, rather than claiming the invention of a new genus of antibodies. [ECF No. 347 at 18]. Although Teva acknowledges that no humanized or human anti-CGRP antibody had been created or tested in the prior art prior to 2005–2006, [ECF No. 400 ¶ 155], it nevertheless contends that it is not claiming a "new" genus of antibodies because, as Lilly argued and the PTAB found, as of 2005–2006 anti-CGRP antagonist antibodies were "well known in the art," and the methods of preparing them were "routine." [ECF No. 347 at 26].

Lilly relies heavily on AbbVie, in which the Federal Circuit affirmed a verdict of invalidity for lack of written description because the patent disclosed one very limited subgenus within a diverse claimed genus. AbbVie, 759 F.3d 1285, 1300–01 (Fed. Cir. 2014). There, the patent claimed a genus of antibodies having a neutralizing function with respect to a particular antigen. Id. at 1299. The patent disclosed several antibodies that served the claimed function and shared a particular structure, that included a 90% or more amino acid sequence similarity in the variable regions. Id. at 1291, 1300. The defendant, however, created an antibody (the accused antibody) that shared the function but differed greatly in structure (*e.g.*, it had about 50% sequence similarity with the asserted antibodies). Id. at 1300. The patentee's experts also "conceded that the [asserted patents] d[id] not disclose structural features common to the members of the claimed genus[,]" id. at 1299, and "d[id] not describe any example, or even the possibility, of [the antibodies] having heavy and light chains other than the [disclosed] types."

Id. at 1300. The court thus concluded that "the claimed genus covers structurally diverse antibodies," id., and that the written description requirement was not met because the patent disclosed no species representative of the structural breadth demonstrated by the accused antibody, id. at 1300–01.

Teva disputes that it has claimed a new genus, but argues in the alternative that even if the specification is required to describe the full genus of anti-CGRP antagonist antibodies used in the claimed methods, a reasonable factfinder could conclude that, taking into account the prior art, the specification's disclosure of Antibody G1, 84 variants of Antibody G1, and seven murine anti-CGRP antagonist antibodies is sufficient to show possession of the entire genus. [ECF No. 347 at 24–25]. Teva relies on Abbott GmbH & Co., KG v. Centocor Ortho Biotech, Inc., 870 F. Supp. 2d 206 (D. Mass. 2012), which involved claims to a "functionally-defined genus . . . of antibodies [defined by] their ability to bind to and neutralize" certain proteins. Id. at 233. The accused infringer argued that "the patents' disclosure of a limited number of representative examples of antibodies within each family [was] an insufficient written description to support the[] genus claims." Id. The Abbott court reiterated that there is no bright line number of species that must be disclosed to satisfy the written description requirement. Id. It further observed that some courts have found that a written description is invalid as a matter of law where the patent fails to disclose a single species of the claimed genus but, in other circumstances, disclosure of "a single representative embodiment may . . . be sufficient to describe a functionally-defined genus." Id. at 234 (citation omitted). The court ultimately found that where the patents at issue disclosed 50 antibodies within the scope of the genus claims that was sufficient to preclude summary judgment. Id. The court noted that the disclosed antibodies "represent[ed] a narrower class than the claimed genuses because the genuses encompass[ed] a

varied range of amino-acid sequences," and the disclosed antibodies "all derived from a single 'lineage'" and had highly similar amino-acid sequences. Id. Nonetheless, "because the parties' experts dispute[d] the significance of the differences in amino-acid sequences" relied upon by the accused infringer, the court found that summary judgment was inappropriate. Id. at 235.

The facts of the present case hew closer to Abbott than AbbVie. Even assuming that Teva is required to disclose sufficient species representative of the genus of claimed antibodies, the record is replete with conflicting evidence, including contradictory expert testimony, regarding (1) the significance of amino acid sequences as compared to antibody structure, (2) the functional similarity between the antibodies disclosed in the patents and Galcanezumab, and (3) the diversity of antibodies disclosed in the prior art. The Court discusses each in turn.

First, Teva and its experts dispute whether the use of amino acid sequences is an appropriate comparison to determine whether the disclosed antibodies were representative of the genus. See [ECF No. 347 at 30–31]. Teva's expert testified that the anti-CGRP antibodies have well-known common structural features, including, among others, a Y-shaped structure and the formation of binding sites (*i.e.*, paratopes) that are structurally complementary to the target antigen. [ECF No. 411 ¶¶ 153, P77]. Additionally, Teva argues that the disclosed antibodies do in fact encompass Galcanezumab's structure because Galcanezumab also contains six CDRs and two variable domains, despite having different amino acid sequences. [ECF No. 360 at 6].

Second, the parties dispute the functional similarity, or dissimilarity, between Antibody G1 and Galcanezumab, which bears on the written description analysis. [ECF No. 294 at 7–8]. In particular, if the patents disclose antibodies that encompass the function of Galcanezumab, that determination would weigh in favor of finding an adequate written description. On the other hand, if Galcanezumab is determined to be functionally different, that would weigh in favor of

invalidating the patents. Lilly claims that the antibodies have clearly distinct functions because Galcanezumab binds to the mid-region of CGRP whereas Antibody G1 binds to the C-terminal end. [Id. at 7]. Teva and its experts contend, however, that the antibodies "are not functionally different because binding to one of those regions rather than the other does not affect whether the antibody will block CGRP's biological function." [ECF No. 347 at 29; ECF No. 400 ¶ P153].

Third, there is conflicting evidence regarding the type of antibodies disclosed in the Patents-in-Suit and in the prior art. Lilly argues that Teva has only disclosed anti-CGRP antagonist antibodies that bind to the C-terminal end of CGRP, but Teva contends that in addition to Antibody G1, the variants, and the murine anti-CGRP antagonist antibodies, its specification also disclosed, through its reference to Tan 1995, anti-CGRP antibodies that bind to the N-terminal region of CGRP. [ECF No. 400 ¶¶ 197, P67–70]. Teva additionally claims that the techniques used to make, screen, and humanize anti-CGRP antibodies were well-known in the prior art, which decreases the number of species of antibodies they needed to disclose to satisfy the written description requirement. [ECF No. 347 at 21–24]. Given this dispute, the Court cannot conclude, that Teva's "patents d[id] not describe any example, or even the possibility, of [the antibodies] having heavy and light chains other than the [disclosed] types," AbbVie, 759 F.3d at 1300, and will not grant summary judgment based on insufficient disclosure of representative species.

ii. Remaining Arguments

This conclusion does not end the analysis, however, because Lilly asserts that Teva's patents further fail the written description requirement because (1) the patents claim types of antibodies that the named inventors tried but failed to make, (2) the specification fails to demonstrate possession of the claimed methods of treatment, and (3) the specification does not

contain information that would permit a POSA to conclude that the antibodies disclosed could cross the BBB and thus treat headache. [ECF No. 294 at 7–9]. Teva, however, disputes each of Lilly's carguments. [ECF No. 347 at 7].

Regarding whether the named inventors tried but failed to make anti-CGRP antagonist antibodies that bound to CGRP's N-terminal end or mid-region and therefore did not possess what they claimed, Teva argues that Lilly is wrong on the law and the facts. [ECF No. 347 at 31]. The Court finds that it need not reach Lilly's legal argument because there is a genuine dispute of fact, namely, whether the inventors tried and failed to make antibodies that bound to regions other than the C-terminal meaning that they did not possess what they claimed or, as Teva alleges, merely discontinued their research due to the acquisition of the research organization (Rinat) by Pfizer. Cf. [ECF No. 400 ¶ 287–89] with [id. ¶ P161–66 ("By late 2006, the named inventors of the '045 patent were 'well underway' to making antibodies that bound to the N-terminus and 'linker region' (*i.e.*, mid-region) of CGRP. Early characterization showed that at least one was an anti-CGRP antagonist antibody (*i.e.*, antagonized CGRP biological activity). The inventors 'did not fully complete the analysis' because their research organization (Rinat) had just been acquired by Pfizer and 'the focus towards generating more anti-CGRP antibodies had shifted.'") (quoting ECF Nos. 368-19 at 179; and 368-27 at 223:1–8, 223:18-224:7) (internal citations omitted)].

The parties also dispute whether the specification describes the claimed methods. Lilly argues that the specification is insufficient because it does not disclose any specific method tailored to treat headache disorder and instead merely suggests various routes of administration, leaving it up to a future POSA to determine an "effective amount" of antibody to be used for treatment based on several factors. [ECF No. 290-1 at 25–26]. Thus, according to Lilly, a

POSA would not have believed that the named inventors possessed a treatment for each listed headache disorder. See [id. at 29–30]. In response, Teva claims that the specification demonstrates that the inventors did possess the claimed methods because, in part, it discloses data from two animal assays that would be understood by a POSA to demonstrate that Antibody G1 would be effective at treating migraine in humans. [ECF No. 347 at 33–34].

Although Lilly claims that several cases support its position, including Ariad, Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004), and FWP IP ApS v. Biogen MA Inc., 749 F. App'x 969 (Fed. Cir. 2018), none of these cases are availing. In Ariad, the full extent of the specification's disclosure was an assertion that the claimed molecules would function as intended and accomplish the desired result. Ariad, 598 F.3d at 1357. The Federal Circuit held that even though "[p]rophetic examples are routinely used in the chemical arts, and [] certainly can be sufficient to satisfy the written description requirement[,]" the disclosure at issue was merely a mention of a desired outcome with "no descriptive link" between the molecules and the desired result. Id. Here, in contrast, the specification disclosed the results from two animal assays that, according to Teva, would be understood by a POSA to demonstrate that the antibodies would be useful for treating headache. [ECF No. 347 at 33–34]. The alleged positive results from *in vivo* tests are, in the Court's view, much more than a bare assertion that a claimed invention will work absent supporting data.

In Rochester, the court affirmed summary judgment for no written description because the patent "does not provide any guidance that would steer the skilled practitioner toward compounds that can be used to carry out the claimed methods . . . and has not provided evidence that any such compounds were otherwise within the knowledge of a person or ordinary skill in the art . . . ." 358 F.3d at 929. The specification at issue here, however, is a far cry from what

the Rochester court confronted. The specification discloses Antibody G1 as well as the results of the *in vivo* animal tests that would purportedly indicate to a POSA that Antibody G1 works in the claimed method. It further discloses prior art references that discuss anti-CGRP antibodies and, as the PTAB concluded, anti-CGRP antagonist antibodies were "well-known" in the prior art. The Court therefore concludes that, unlike in Rochester, the specification's disclosure does direct a POSA toward compounds that can be used in the claimed methods.

Finally, in FWP IP, the court held that the written description was inadequate where the specification did not demonstrate that the claimed compounds "were in fact effective for treating the entire list of enumerated conditions" which was presented as a "laundry list of diseases and conditions include[ing] psoriasis; psoriatic arthritis; neurodermatitis; inflammatory bowel disease; neurodermatitus; autoimmune diseases (including [multiple sclerosis] as one of the eleven listed); pain associated with radibulopahty, neuropathy, or sciatica; organ transplantation" and several more. 749 F. App'x 969, 972, 975 (Fed. Cir. 2018). This case is easily distinguishable because the list in FWP IP included a far greater variety of diseases that the claimed invention purported to treat, as opposed to the present case where the condition to be treated was "headache." Moreover, Teva contends that the two *in vivo* assays do demonstrate the effectiveness of its claimed inventions, which further distinguishes the present case from FWP IP where the specification did not demonstrate that the claimed compounds were effective. At minimum, there remains a genuine dispute over the extent of the specification's disclosure.

Accordingly, based on the numerous factual disputes discussed above, the court denies Lilly's motion for summary judgment for lack of written description.

F. Lack of Enablement

Lilly argues that Teva's asserted patents are not enabled because it would require undue experimentation to (1) make the full scope of functionally-defined antibodies referenced in the claims and (2) use the antibodies in the claimed method. [ECF No. 290 at 7–8]. Teva responds that practicing the full scope of the claims does not require undue experimentation and, at the very least, there are genuine disputes of fact as to whether the claims are enabled. [ECF No. 353 8–10].

"The requirement of enablement, stated in 35 U.S.C. § 112, enforces the essential '*quid pro quo* of the patent bargain" by requiring a patentee to teach the public how 'to practice the full scope of the claimed invention." McRO, Inc. v. Bandai Namco Games Am., Inc., 959 F.3d 1091, 1099–100 (Fed. Cir. 2020) (quoting AK Steel Corp. v. Sollac, 344 F.3d 1234, 1244 (Fed. Cir. 2003)). "To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" Amgen Inc. v. Sanofi, Aventisub LLC, 987 F.3d 1080, 1084 (Fed. Cir. 2021) (quoting Alcon Rsch. Ltd. v. Barr Lab'ys, Inc., 745 F.3d 1180, 1188 (Fed. Cir. 2014)). "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). The factual consideration, known as the "Wands factors," are:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id.

Lilly first argues that Teva's claims are not enabled because they do not provide the amino acid sequences for all the antibodies that have the function of binding to CGRP, inhibiting CGRP biological activity, and, in turn, treating migraine or other headache disorders. [ECF No. 290 at 19]. As a result, undue experimentation becomes necessary as the number of possible antibodies is so enormous that modifying the amino acids only within the CDRs of a single antibody "results in 5 x 10^{80} antibodies—***more than the number of stars in our galaxy*** ($1x10^{11}$)***, atoms in the Earth*** ($1x10^{51}$)***, or hydrogen atoms in the universe*** ($4x10^{79}$)." [Id. at 20]. Lilly also claims that "A POSA Had No Prior Experience with the Claimed Antibodies in This New Field" and "would have had ***no experience*** with the claimed methods" and would therefore have to undertake undue experimentation. [Id. at 22].

The Court finds that Lilly has failed to carry its burden to show that there is no genuine dispute of material fact as to whether a POSA would need to engage in undue experimentation, as opposed to routine experimentation, to make the antibodies used in the claimed methods. This is true even assuming, as Lilly argues, that Teva has claimed all humanized or human anti-CGRP antagonist antibodies. "Undue experimentation is a matter of degree. Even a considerable amount of experimentation is permissible, as long as it is merely routine or the specification provides a reasonable amount of guidance regarding the direction of experimentation." Wyeth & Cordis Corp. v. Abbott Lab'ys, 720 F.3d 1380, 1385–86 (Fed. Cir. 2013) (internal citations and quotation marks omitted). Here, the parties agree that the relevant POSA has either a Ph.D. in a field such as immunology, biochemistry, or pharmacology with several years of post-doctoral experience in antibody engineering, pharmacokinetics, and pharmacodynamics, or is a M.D. with a residency or specialty in neurology, and several years of experience studying CGRP or treating patients with a headache disorder such as migraine. [ECF No. 411 ¶¶ 223–24]. Given this high

degree of expertise, Lilly's argument focusing on the immense possible diversity of antibodies resulting from the randomization of every amino acid in every CDR in a single antibody is of no moment. The suggestion that someone with that degree of knowledge would engage in such a dramatic and disorganized substitution in search of an antibody that binds to and antagonizes CGRP is not credible or persuasive.

Moreover, Teva has presented substantial evidence that the state of the prior art of antibody engineering was advanced and predictable, the relative skill of those in the art was high, and any experimentation needed to practice the claimed invention was "routine" and "conventional." As just one example, the evidence proffered by Teva suggests that screening to identify CGRP antagonist antibodies was accomplished via automated, high-throughput, commercially available assays. [ECF No. 411 ¶¶ P68–P73]. Moreover, as Lilly itself argued and the PTAB agreed, by 2005–2006, anti-CGRP antagonist antibodies were well known in the prior art. [ECF No. 411 ¶ 14].

Lilly's next argues that because the asserted claims encompass administering an effective amount of any anti-CGRP antagonist antibody to treat one of numerous headache disorders, the specification amounts to an invitation for further research and experimentation. [ECF No. 290 at 24–25]. Further, because as of 2005–2006 a POSA would have had no experience using the claimed antibodies to treat headache, extensive trial-and-error experimentation and clinical trials would be necessary to practice the claimed methods. [Id. at 25]. Here, again, the Court finds that Lilly fails to carry its burden. Among others, the parties dispute (1) whether a POSA would be starting from a blank slate when identifying an effective amount to treat headache, (2) whether the specification provided sufficient guidance on dosing, (3) whether Teva needed to provide dosing regimens for each of the sub-types of headache disorders listed in the

specification, (4) whether the only headaches linked to CGRP were migraines and some forms of cluster headaches, and (5) whether testing in humans was essential to practice the claimed methods. These numerous factual disputes reflect that summary judgment is wholly inappropriate on the issue, and Lilly's motion for summary judgment for lack of enablement is therefore denied.

IV. CONCLUSION

Accordingly, Lilly's motions for summary judgment for lack of enablement, insufficient written description, and no willful infringement are DENIED, its partial motion for summary judgment for non-infringement is GRANTED and Teva's motions for summary judgment regarding judicial estoppel and inequitable conduct are DENIED.

SO ORDERED.

October 3, 2022

/s/ Allison D. Burroughs
ALLISON D. BURROUGHS
U.S. DISTRICT JUDGE