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IN THE UNITED STATES DISTRICT COURT

FOR THE CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

GENZYME CORPORATION,

Plaintiff,

v.

GENENTECH, INC., and CITY OF HOPE

Defendants.

GENENTECH, INC., and CITY OF HOPE,

Counter-Plaintiffs,

v.

GENZYME CORPORATION

Counter-Defendant.

Case No. 2:15-cv-09991-GW-AGR

**DEFENDANTS' RESPONSIVE CLAIM CONSTRUCTION BRIEF**

Ctrm: 10, Spring Street Floor
Judge: George H. Wu

**JURY TRIAL DEMANDED**

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## I. INTRODUCTION

Genzyme's opening claim construction brief does not dispute that Defendants' construction reflects the plain and ordinary meaning of "variable region": "the N-terminal end of a heavy or light chain that terminates before the beginning of the constant region." Nor does Genzyme point to anything in the claim language or specification that would support its own proposed construction. To the contrary, Genzyme acknowledges that the claims on their face are "broad enough to encompass" precisely the claim scope Genzyme seeks to exclude to support its noninfringement position. Genzyme Opening Br. at 14. Instead, Genzyme's ***only*** support for its argument that the claims should be narrowed to exclude Genzyme's Lemtrada® product is prosecution history disclaimer. But, as demonstrated below, that prosecution history simply cannot bear the weight Genzyme places on it. Genentech did not disclaim claim scope or acquiesce to rejections by the Examiner. To the contrary, it consistently and clearly put the Examiner—and the public—on notice that the claims should be entitled to their full scope. And, while Genzyme now takes issue with the assertion that the Cabilly III patent claims cover Genzyme's product Lemtrada® in view of the fact that Lemtrada® is "a 'humanized' antibody that is 'altered' by combining human and nonhuman DNA sequences," Genzyme paid royalties on that antibody under the Cabilly III patent without suggesting that Genzyme did not require such a license.[1] Genzyme's claim construction position should be rejected.

## II. THE SOLE CLAIM CONSTRUCTION DISPUTE: "VARIABLE REGION"

### A. There Is No Dispute That Defendants' Construction Accurately Defines The Ordinary Meaning Of A Variable Region

As explained in Defendants' opening brief, variable regions are the ends of the heavy or light chains that terminate before the beginning of the constant region. *See*

[1] The Cabilly III patent issued on April 12, 2011. Lemtrada® was approved on Nov. 14, 2014 and Genzyme paid royalties on Lemtrada® until Sept. 30, 2015. Joint Stipulation to Allow Genentech, Inc. and City of Hope to File Answer and First Amended Counterclaims against Genzyme, Inc. at 1, ECF No. 71.

Defendants' Opening Brief at 10-11. Genzyme's opening brief does not take issue with this ordinary meaning. *See* Genzyme Opening Brief at 5 (including figure showing variable regions at the end of the heavy and light chains and terminating before constant region); *see also id.* at 19 (noting "Defendants' proposed construction is 'the N-terminal end of a heavy or light chain that terminates before the beginning of the constant region,' which Genzyme assumes is intended by Defendants to be the ordinary and customary meaning of 'variable region[,]'" while failing to challenge this ordinary meaning).[2]

### B. There Is No Dispute The Claim Language And Specification Support Defendants' Proposed Construction

It is black-letter law that claim construction begins with the language of the claim itself. *See, e.g.*, *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). Genzyme's claim construction analysis does not. To the contrary, Genzyme elects not to tackle the claim language (or the specification of which it is a part) as part of the claim construction analysis. The only real discussion of the scope of the claim language and specification is buried in the background section of Genzyme's opening brief. There, Genzyme ***admits*** that the claim language and specification support Defendants' proposed construction, and, absent a finding of prosecution history disclaimer, are broad enough to encompass the scope that Genzyme seeks to read out of the claims.

With respect to the claim language itself—the touchstone for any claim construction analysis—Genzyme acknowledges that the claim language supports Defendants' interpretation and "permits" the claim scope at issue here:

[2] In co-pending litigation, Dr. Jefferson Foote, expert witness for Sanofi and Regeneron (Genzyme's corporate relatives, represented by the same counsel) confirmed Genentech's reading of the claims. *See* Supplemental Declaration of Adam R. Brausa submitted herewith ("Brausa Suppl. Decl."), Ex. 14, Foote Dep. Tr. at 49:7-14 (322) ("Q. So is it your understanding that in claim 25 of the Cabilly III patent the variable region could be from any species or any source so long as it is -- has specificity for a desired antigen? Yes. This doesn't restrict it to any species.") (objection omitted); *see also id.* at 57:9-16 (324) ("Q. And would you agree that, just as that term is used in claim 25 of the Cabilly III patent, that variable region – there's no restrictions placed on what that variable region could be? It's not restricted in here, yes.") (objection omitted).

> While the constant region must be wholly human, the word "comprising" preceding the description of the variable region permits an interpretation that the ***variable region may contain human amino acid sequences in addition to the expressly required non-human mammalian sequences***.[6]
>
> [6] "Comprising" is considered an "inclusive" or "open-ended" term that "does not exclude additional, unrecited elements." *CollegeNet, Inc. v. ApplyYourself, Inc.*, 418 F.3d 1225, 1235 (Fed. Cir. 2005).
>
> Claims 25, 26, 38 and 47 (and their dependent claims) all recite "a variable region sequence" without reference to the species (human, non-human, or both) source of the amino acid sequence. . . . These claims on their face are therefore ***broad enough to encompass variable regions with part-human/part-murine or otherwise altered sequences***.

Genzyme Opening Br. at 13-14.[3]

Beyond the claims, the specification "is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). Genzyme also does not dispute that the specification confirms this natural reading of the claims. Indeed, Genzyme cites to some of the same disclosures of chimeric and altered antibodies that Defendants detailed in their opening brief. Genzyme Opening Br. at 14-15. For example, Defendants' opening brief explained that the specification discloses antibodies with sequences that have been altered or varied from the sequence of a vertebrate antibody: "'[a]ltered antibodies' means antibodies wherein the amino acid sequence has been varied from that a mammalian or other vertebrate antibody." Cabilly III Patent at 6:66-7:1 (53-54), ECF No. 75-3. The patent contemplates that "[c]hanges in the variable region will be made in order to improve the antigen binding characteristics." *Id.* at 7:11-12 (54). Likewise, the specification defines chimeric antibodies as "antibodies wherein one portion of each of the amino acid sequences of heavy and light chains is homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular class, while the remaining segment of the chains is homologous to corresponding sequences in another." *Id.* at 6:30-35 (53). And the specification goes on to make clear that the Cabilly invention is not limited to chimeric antibodies with human constant domains and non-human variable domains. Instead, the Cabilly invention

[3] Emphasis supplied and internal citations omitted throughout, unless otherwise noted.

includes any antibody with combinations of sequences from different sources:

> However, ***the definition is not limited to this particular example***. It ***includes any antibody*** in which either or both of the heavy or light chains are composed of ***combinations of sequences mimicking the sequences in antibodies of different sources***, whether these sources be differing classes, differing antigen responses, or ***differing species of origin and whether or not the fusion point is at the variable/constant boundary***. Thus, it is possible to produce antibodies in which neither the constant nor the variable region mimic known antibody sequences. It then becomes possible, for example, to construct antibodies whose variable region has a higher specific affinity for a particular antigen, or whose constant region can elicit enhanced complement fixation or to make other improvements in properties possessed by a particular constant region.

*Id.* at 6:51-65 (53).

Genzyme does not dispute that its proposed construction is directly at odds with these disclosures. Nor could it. Instead, Genzyme argues only that the claims and specification cover variable regions with alterations that it contends are unsupported by experimental examples and extend beyond what was possible or predictable in April 1983. *See* Genzyme Opening Br. at 14-15. In other words, Genzyme is challenging the specification's ***enablement*** of the claims, not its disclosure. Enablement is a separate question from claim construction and will be addressed later in the litigation. *See, e.g.*, *Phillips*, 415 F.3d at 1327 ("While we have acknowledged the maxim that claims should be construed to preserve their validity, we have not applied that principle broadly, and we have certainly not endorsed a regime in which validity analysis is a regular component of claim construction. Instead, we have limited the maxim to cases in which 'the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous.' In such cases, we have looked to whether it is reasonable to infer that the PTO would not have issued an invalid patent, and that the ambiguity in the claim language should therefore be resolved in a manner that would preserve the patent's

validity."). Here, the scope of the claims is clear and undisputed.[4]

### C. Genzyme's Prosecution History Disclaimer Theory Fails

With the claims and specification providing no legitimate basis to depart from the agreed-upon ordinary meaning of "variable region" or otherwise restrict the Cabilly III patent to support Genzyme's noninfringement position, Genzyme relies exclusively on the prosecution history to support its attempt to narrow the claims. As shown below, the prosecution history does not reflect any disclaimer, let alone a "clear and unmistakable" one.

#### 1. Genzyme Misconstrues The Prosecution History

In its opening brief, Genzyme paints a picture of the file history of the Cabilly III patent with the goal of proving that Genentech was forced to disclaim the claim scope that Genzyme is now seeking to exclude (i.e., antibodies with variable regions that do not entirely mimic sequences that are found in nature) and that Genentech acquiesced to that disclaimer to obtain the patent. In so doing, Genzyme glosses over the significant complexities in the prosecution history, the shifting nature of the claims at issue, and

[4] Enablement is tested as of the filing date of the Cabilly III patent, here April 1983. As Defendants will ultimately prove (when the issue is properly before the Court), the claims of Cabilly III are directed to a method of making the heavy and light chains of an antibody that can be used to make chains corresponding to any available DNA sequence, including DNA sequences that have been manipulated to vary from sequences found in nature. The Cabilly disclosure enables the full scope of that claim, and nothing about the Cabilly method itself depends in any way on the DNA sequence that is being expressed (i.e., the specific composition or source of the heavy or light chains). Moreover, the specification contains a detailed teaching of how to make chimeric antibodies (which the specification describes as including antibodies with junctions at various points including within the variable region) using the Cabilly III invention. ECF No.75-3, Cabilly III patent at 26:10-27:51 (63-64). It also contains a detailed discussion of altered antibodies with various alterations in the DNA sequence that can be made "by standard recombinant techniques and also by oligonucleotide-directed mutagenesis techniques." *Id*. at 6:66-7:18 (53-54) (citing publications). Genzyme tries to make hay of the fact that Genentech argued, in the *Chiron v. Genentech* case, that the making of a humanized antibodies was unpredictable as of 1986. Genzyme Opening Brief at 24 n.10. However, in *Chiron*, the court specifically found that Chiron was ***not*** required to enable "humanized antibodies" as defined in the parlance of that case (antibodies resulting from specific modifications that were described in 1986) because those precise antibodies were not known as of the filing date of the patent at issue in that case, i.e., they were found to be after-developed technology. *Chiron Corp. v. Genentech, Inc*., 363 F.3d 1247, 1251, 1354 (Fed. Cir. 2004).

Genentech's repeated explanation that they were not acquiescing in any of the Examiner's assertions, none of which were even directed to the application claims that ultimately issued.[5]

To start, Genzyme's prosecution history disclaimer focuses on claim 53 of the application that later issued as the Cabilly III patent. As proposed, Claim 53 read:

> A process for producing an altered antibody heavy or light chain, or a fragment thereof, comprising the steps of
>
> a) transforming a recombinant host cell with a replicable expression vector comprising a DNA sequence encoding an altered antibody heavy or light chain or a fragment thereof having specificity for a particular desired antigen, the amino acid sequence of which has been varied from that a of a natural mammalian immunoglobulin heavy or light chain or a fragment thereof by alteration deletion or addition of one or more predetermined amino acid residues;
>
> b) culturing the host cell to produce a host cell culture; and
>
> c) recovering the altered antibody heavy or light chain from the host cell culture.

*See* ECF No.75-7, July 7, 1995 Preliminary Amendment at 1-2 (223-24).

Genzyme points out that, following an office action rejecting the claims under the enablement requirement of Section 112 and over the prior art under Section 102, Genentech amended Claim 53 to add the underlined language: "A process for producing an altered antibody heavy or light chain, or a fragment thereof <u>having variable and constant region sequences</u>, comprising the steps of a) transforming a recombinant host cell with a replicable expression vector comprising a DNA sequence encoding an altered antibody heavy or light chain or a fragment thereof having specificity for a particular desired antigen, . . . ." *See* ECF No. 75-10, March 20, 1997 Amendment at 1 (234).

But Genzyme omits that, in amending its claims, Genentech made clear that it "disagree[d] with the Examiner's position," and "vigorously" denied both the objection to the specification and the rejection of the claims under this section. *Id.* at 3 (236). Genentech went on to provide five pages of argument on the enablement issue, explaining

[5] A detailed summary of the prosecution history is set forth in Defendants' Opening Brief. *See* Defendants' Opening Br. at 16-21.

that the rejection was based on the Examiner's improper "reading of the term 'altered antibody', which is not supported by the plain meaning of the claims, or by the definition provided in the specification." *Id.* at 4 (237). The Examiner had read "altered antibody" to include alterations to the antibody that were not based on the DNA sequence encoding for the antibody, but instead reflected changes to the protein structure that might take place after the fact. Genentech explained that, contrary to the Examiner's reading, "Claim 53, on which all claims under examination depend, defines a process for making altered antibody heavy or light chains or fragments of such chains (provided that such fragments contain constant region sequences), by expressing, in a recombinant host cell, a DNA sequence which encodes an antibody chain or chain fragment, the amino acid sequence of ***which has been varied from that of a natural mammalian immunoglobulin heavy or light chain or chain fragment, by the alteration, deletion or addition of one or more amino acids***." *Id.* "This language is clear in that the alteration must be in the amino acid sequence of a native antibody or antibody fragment, and that such alteration is produced by a corresponding alteration in the underlying DNA sequence." *Id.*

Genentech went on to point the Examiner to the "definition provided in the specification for altered antibodies," which "shows that altered antibodies are made by 'suitable amino acid alterations, deletions or additions[.]'" ECF No. 75-10 at 4 (237). With respect to changes in the amino acid sequences in the variable region specifically, Genentech argued that specification, coupled with the prior art, provided precisely the required enabling disclosure: "[e]quipped with this knowledge, a person skilled in the art was in a position to ***make alterations within (and outside) the hypervariable regions [CDRs] of an antibody***, and obtain variant antibodies with improved or otherwise altered antigen binding properties. As the hypervariable regions are of limited lengths, once the present invention was made, a person skilled in the art was ***able to make changes within the variable regions of an antibody***, and test the consequences of such changes, without undue experimentation." *Id.* at 5-6 (238-39).

None of this context surrounding the amendment is acknowledged, let alone addressed, by Genzyme. Instead, Genzyme goes on to rely heavily on the next Office Action and Genentech's response thereto. Genzyme Opening Brief at 17-18. Genzyme is right that, following another rejection, Genentech amended Claim 53 and cancelled Claims 54-66 in favor of new Claims 81-88. *See* ECF No. 75-11, Jan. 12, 1998 Amendment (244-54). But again, Genzyme omits that Genentech proposed a number of changes to Claim 53, noting that "[a]lso ***without acquiescing*** in the Examiner's position, claim 53 has been amended to recite the production of antibodies comprising chimeric immunoglobulin heavy and light chains. The ***rejection of claim 53*** and any anticipated rejection of newly added claims 81 to 88 is ***vigorously traversed***." *Id.* at 6 (249). Genentech provided a detailed technical explanation to demonstrate that "claims 53 and the dependent claims are ***enabled within their full scope***." *Id.* at 10 (253).

Again, Genzyme fails to acknowledge, let alone address, how these statements can be squared with Genzyme's allegation that Genentech clearly and unmistakably disavowed claim scope or acquiesced to anything. Also notably absent from Genzyme's discussion of the file history is any discussion of the subsequent prosecution history, including in particular the examination surrounding the claims that actually issued with the patent. Instead, Genzyme devotes a single, conclusory paragraph to the events that took place between January 1998 and the patent's issuance over a decade later. Genzyme Opening Brief at 18. Here is what Genzyme skipped.

After another rejection, Genentech made a further amendment. *See* ECF No. 75-12, Jan. 6, 1999 Amendment. In this amendment, Genentech cancelled Claim 53 in favor of new Claim 89, and proposed amendments to pending Claim 67. In relevant part, Claim 89 included the requirement of "[a] process for producing an immunoglobulin capable of specifically binding a desired antigen, said immunoglobulin comprising chimeric heavy and light immunoglobulin polypeptide chains each having a human constant region sequence and a non-human mammalian variable region sequences. . . ." *Id.* at 3 (257). Claim 67 was amended to add the requirement of "a human constant region sequence and

a non-human mammalian variable region sequences." *Id.* at 1-2 (255-56). Once again, Genentech made clear that its amendments were made to facilitate prosecution and not intended to suggest any acquiescence to the amendment or disclaimer of claim scope. *Id.* at 5 (259) ("***Purely in the interests of expediting prosecution and without acquiescing in the rejection***, Applicants have revised claim 67 to state that the heavy chain, light chain or fragment thereof has 'a human constant region sequence and non-human mammalian variable region sequences.'"); *id.* at 4 (258) ("***In the interests of expediting prosecution and without acquiescing in the rejection***, claim 89 (which corresponds to rejected claim 53) has been amended to refer to an immunoglobulin capable of specifically binding a 'desired' antigen as suggested by the Examiner and the offending language 'in appropriate reading frame for production of said chains' and 'wherein, if the immunoglobulin is deposited within the cells as insoluble particles, the mature heavy or light chains are recovered from the particles by cell lysis followed by solubilization in denaturant and reconstitution of the immunoglobulin" has been removed from the claim."). Neither of these amendments or the related discussion related in any way to the alleged disclaimer.

After further rejections and interviews, Genentech again amended its claims. *See* Brausa Suppl. Decl. Ex. 15, Oct. 1, 1999 Amendment at 1-2 (388-89). Genentech cancelled all pending claims "***without prejudice or disclaimer,***" and proposed new claims 90-114 that recited antibody heavy chains or fragments and light chains or fragments that "comprise[] a human constant region sequence and a variable region comprising non human mammalian variable region sequences." *Id.* In submitting this Amendment, Genentech addressed these new claims, explaining why they did not present new matter and how they were enabled, citing the declaration of Nobel Laureate Richard Axel in support of enablement. *See id.* at 7-12 (394-99). On November 18, 1999, the Patent Office issued a Notice of Allowability allowing the later-added claims as originally proposed on October 1, 1999. *See* Brausa Suppl. Decl. Ex. 16, Nov. 18, 1999 Notice of Allowability (401) (allowing claims 90-114 in the application because "[u]pon reconsideration of applicant's added claims, filed 10/5/99 including the Axel declaration

under 37 C.F.R. § 1.132 (Paper Nos. 31132); the pending claims are deemed allowable").

After a lengthy interference proceeding in which Genentech prevailed, Genentech presented allowed claims 90-114 and new claims 115-138. *See* ECF No. 75-5, July 12, 2010 Amendment. Those new claims introduced for the first the requirement of heavy and light chains or fragments "comprising a variable region sequence and a human constant region sequence." *See id.* at 6-10 (294-98). In connection with these new claims, Genentech explained "[t]he claims are similar in form to allowed claims 90 to 109 and 111-114, respectively, but refer to 'a variable region sequence and a human constant region sequence' as supported *inter alia*, at page 3, line 10, page 11, lines 4-9, and page 12, lines 6-7 of the specification. Applicants have previously identified the various bases of support for the allowed claims, which also support the amended claims." *Id.* at 11 (299). And previously, Genentech specifically referred the Examiner to the discussion of chimeric and altered antibodies in the specification as support for these new claims. ECF No. 75-12, Jan. 6, 1999 Amendment at 12-13 (266-67).

The Patent Examiner issued an Examiner's amendment cancelling claims 110 and 134, but otherwise allowing claims 90-138 without amendment or further argument. *See* ECF No. 75-16, Dec. 21, 2010 Notice of Allowability. Those claims issued as claims 1-47 of the Cabilly III patent. However, in attempting to narrow the scope of these claims through prosecution history disclaimer, Genzyme failed to address the statements made about the actual claims at issue at all.

**2. There Was No Clear And Unmistakable Disavowal During Prosecution**

The prosecution history of a patent plays various roles in resolving uncertainties about claim scope. *Phillips*, 415 F.3d at 1317. Where, as here, the prosecution history is used solely to support a conclusion of patentee disclaimer, the standard for disclaimer is a high one. "[T]he prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, [and] often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.*

Thus "for prosecution disclaimer to attach, our precedent requires that the alleged disavowing actions or statements made during prosecution be ***both clear and unmistakable***." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325–26 (Fed. Cir. 2003); *see also Storage Tech. Corp. v. Cisco Sys., Inc.*, 329 F.3d 823, 833 (Fed. Cir. 2003) ("We therefore do not consider the applicants' statement to be a clear and unambiguous disavowal of claim scope as required to depart from the meaning of the term provided by the written description."); *see also, e.g., Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1369 (Fed. Cir. 2003).

Importantly, "[t]here is no 'clear and unmistakable' disclaimer if a prosecution argument is subject to more than one reasonable interpretation, one of which is consistent with a proffered meaning of the disputed term." *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1287 (Fed. Cir. 2005); *Omega Eng'g*, 334 F.3d at 1325 ("[W]e have thus consistently rejected prosecution statements too vague or ambiguous to qualify as a disavowal of claim scope."); *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1359 (Fed. Cir. 2003); *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319, 1327 (Fed. Cir. 2002). To the contrary, the prosecution history does not limit claim scope "unless the applicant took a position before the PTO that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter." *Inverness Med. Switz. GmbH v. Warner Lambert & Co.*, 309 F.3d 1373, 1382 (Fed. Cir. 2002).

Applying these principles, Genzyme's prosecution history disclaimer theory fails at multiple levels.

***First***, Genzyme's theory runs afoul of the requirement "the totality of the prosecution history . . . must be assessed . . . ." *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999); *Biovail Corp. Int'l v. Andrx Pharm., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001) ("Claim language, however, must be read consistently with the totality of the patent's applicable prosecution history."); *Rheox, Inc.*, 276 F.3d at 1326 ("We assess whether a patentee relinquished a particular claim construction based on the totality of the prosecution history, which includes amendments to claims and arguments

made to overcome or distinguish references.").

While Genzyme attempts to gloss over much of it, the Cabilly III patent was subject of a lengthy and rigorous prosecution, and interference proceedings that went on for about a decade. The claim amendments and cancellations that Genzyme relies upon so heavily have to be viewed as part of that broader context. To be sure, certain claims were canceled and various limitations related to the variable region were added as the claims changed over time, but this was part and parcel of other amendments to the claims and, in some cases, involved the proffering of entirely new claims. ***At every turn***, Genentech emphasized that it was not disclaiming claim scope or acquiescing to the Examiner's rejections—and that, instead, its amendments were to expedite prosecution as to particular claims, without prejudice to obtaining claims for the full scope of the invention. Thus, Genentech not only did not take "a position before the PTO that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter[,]" *Inverness Med.*, 309 F.3d at 1382, but it put all its competitors on notice that it was not disclaiming claim scope. This is particularly true because "[i]t is well settled . . . that ***it is the applicant, not the examiner, who must give up or disclaim*** subject matter that would otherwise fall within the scope of the claims." *Innova/Pure Water, Inc., v. Safari Water Filtration Systems, Inc.*, 381 F.3d 1111, 1124 (Fed. Cir. 2004). Thus, whatever the Examiner may have thought at a particular point in time,[6] Genentech was always clear about its position. *See SanDisk Corp.*, 415 F.3d at 1287 ("There is no 'clear and unmistakable' disclaimer if a prosecution argument is subject to more than one reasonable interpretation, one of which is consistent with a proffered meaning of the disputed term.")

[6] During prosecution, Genentech went to great pains to explain why the Examiner's interpretation of "altered antibodies" was improper. *See* ECF No. 75-10, Mar. 20, 1997 Amendment. While Genzyme ignores that part of the prosecution history entirely now, the public notice function of the prosecution history was certainly fulfilled. No competitor could read that file history and reasonably come away with the conclusion that Genentech was disclaiming any claim scope.

Genzyme characterizes *United Video Properties* as "particularly instructive," but that case involved a very different prosecution record. Genzyme Opening Br. at 21-22 (citing *United Video Props., Inc. v. Amazon.com Inc.*, 561 F. App'x 914, 917-18 (Fed. Cir. 2014)). In *United Video Properties*, the patentee amended the claim at issue to remove the language "Internet delivered data," replacing it with "the data feed" to overcome a rejection, noting that the amendment was being made to "more particularly define the invention." *United Video Props.*, 561 F. App'x at 915. The question was whether the "data feed" in the amended claim could be construed to include internet delivered data. Critically, there was no suggestion that the applicant in that case had made an affirmative statement that it was not acquiescing in the examiner's prior rejection (unlike every claim amendment at issue here). According to Genzyme, the Federal Circuit found a disclaimer in *United Video Properties* on a much smaller record of disavowal and surrender than is alleged here because "the patent applicant merely deleted a word from the pending claim." Genzyme Opening Br. at 25. But that actually cuts the other way. This is not a case in which an applicant made a simple claim amendment (i.e., add or remove a word or two) to overcome a rejection, without saying more, such that the applicant's intent to disclaim claim scope is clear. To the contrary, the prosecution history in this case reveals a complex set of claims that evolved over time, with lots of moving parts (including two sets of claims newly added towards the end of prosecution as to which there was no discussion whatsoever of the issues relating to the alleged disclaimer), and explicit statements that the applicant was not acquiescing in the intermediate rejections—and no action or statement amounting to a "***both clear*** and ***unmistakable***" disclaimer.

***Second***, Genzyme's theory is improperly disconnected from the actual claim language at issue. To be sure, claims should be read as part of the overall prosecution history, including claims that have been cancelled or rejected. *Schriber-Schroth Co. v. Cleveland Trust Co.*, 311 U.S. 211, 220-21 (1940). But that goes both ways. One cannot, as Genzyme does, find estoppel based on earlier claim cancellations or amendments without considering the prosecution history relating to the claims that actually issued.

The entirety of Genzyme's analysis regarding the claims that actually issued—the claims that include the "variable region" language now being construed—is limited to a couple of throw-away sentences at the end of its brief. Genzyme Opening Br. at 25. According to Genzyme, "[a]t no time following the cancellation of claims 55 and 56 and the amendment to claim 53 did Defendants make it in any way clear to the Patent Examiner that by filing new claims they intended to reclaim the scope of altered variable regions they had previously disclaimed." *Id.* Not only does this assume there was a disclaimer to begin with (which there was not), but it ignores Genentech's repeated statements that did in fact make it clear (in every way) to the Patent Examiner that it was not disclaiming claim scope. And while Genzyme contends that "[t]he subject of variable region alterations was never mentioned again, and the word 'altered,' or any of its various synonyms, does not appear in any subsequent Amendment filed by the Defendants or in any Office Action entered by the Examiner[,]" *id.*, Genzyme fails to note that the claim language at issue was not part of the claims during the supposed disclaimer. That language (which includes the "variable region" limitation) was part of claims that were proposed, examined, and allowed, including with specific citations to the portions of the specification providing support for the new claims. Genzyme concedes that that claim language on its face covers antibodies with variable regions that do not entirely mimic sequences that are found in nature. Yet there was no rejection by the Examiner as to those claims and no amendment or argument narrowing the claims after they were proposed by Genentech. Thus, whatever may have happened earlier in the prosecution with respect to different claims with different limitations, and whatever confusion there may have been regarding their scope, Genentech's statements throughout prosecution and the subsequent prosecution history make clear that the scope of the later claims continues to cover precisely what Genzyme seeks to exclude.

## III. CONCLUSION

The claimed "variable regions" should be given their ordinary meaning, consistent with both the language of the claims themselves and the specification. Genzyme has not

come close to establishing a "clear and unmistakable disavowal" of claim scope that could support narrowing the claims to exclude antibodies with particular variable region compositions. Genzyme's proposed construction should be rejected.

Dated: July 1, 2016

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**CERTIFICATE OF SERVICE**

I certify that all counsel of record is being served on July 1, 2016 with a copy of this document via the Court's CM/ECF system.

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