In the United States Court of Federal Claims

No. 15-1549C
(E-Filed: April 27, 2018)

UNIVERSITY OF SOUTH FLORIDA, BOARD OF TRUSTEES, Plaintiff, v. THE UNITED STATES, Defendant.	Claim Construction; Markman Hearing; Preamble Construction.

ORDER

In this patent infringement suit, the court has before it the parties' claim construction arguments. See ECF Nos. 69, 69-1 (Jt. Claim Construction Statement and Chart); 75 (plaintiff's initial brief); 76 (defendant's initial brief); 83 (plaintiff's reply brief); 84 (defendant's reply brief). Also before the court is the transcript of the claim construction hearing held on January 31, 2018. See ECF No. 100 (hearing transcript (Tr.)). This order memorializes the court's construction of disputed claim terms in United States Patent No. 5,898,094 ('094 patent).

I. Background

Plaintiff University of South Florida, Board of Trustees (USF) holds the rights to the '094 patent, which is titled "Transgenic Mice Expressing APPK670N,M671L and a Mutant Presenilin Transgenes."[1] ECF No. 76-1 at 2. The invention in the '094 patent is presented in 14 claims. Id. at 11-12. The claims all discuss a "transgenic mouse" or the methods for screening transgenes and/or for preparing the transgenic mice, id., which are also sometimes described

[1] The court will not explain any technical terms of the '094 patent in this order. The claimed mice are genetically modified, i.e., transgenic, so that they develop a feature (or features) that is characteristic of Alzheimer's Disease. The court defers any in-depth discussion of the scientific basis of the '094 patent for further proceedings in this matter.

as "doubly transgenic" mice, id. at 8. Such mice are of utility in the research of Alzheimer's Disease (AD) and other neurodegenerative disorders. Id. at 5.

The parties' positions on claim construction focus on two main controversies, and diverge, as well, as to whether terms in the preambles of the claims require construction. The first controversy is whether the claim terms accelerated and enhanced signify that a characteristic of the transgenic mouse "occurs at least one month earlier in the mouse life span," or merely occurs "earlier in the mouse life span." ECF No. 69-1. The second controversy is whether the phrase Alzheimer's Disease related pathology signifies the development of a three-component cluster of AD characteristics, or less specifically signifies that at least one characteristic of AD, such as "beta-amyloid plaques," is developed in the transgenic mouse. Id. Finally, defendant argues that the language in the preambles of certain claims needs no construction because the preamble language is not limiting. Id.

Of the fourteen claims, the parties have proposed a joint construction of three terms that are found in Claims 1, 3, 5, 7-11, and 13. Id. at 3. The court accepts the parties' proposed undisputed construction of those terms, as set forth in the table attached to this order as Attachment 1. The parties dispute, however, the construction of other terms in Claims 1, 3, 5, 7-11, and 13. There are, however, as stated supra, only two principal claim construction disputes regarding the terms in the fourteen claims in the '094 patent, accompanied by a third question as to whether the preambles of certain claims require construction. The court's resolution of these disputes is also recorded in the table attached to this order.

II. Claim Construction

Claim construction "determin[es] the meaning and scope of the patent claims asserted to be infringed." Markman v. Westview Instruments, Inc., 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc) (citation omitted), aff'd, 517 U.S. 370 (1996). "[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy." Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc., 200 F.3d 795, 803 (Fed. Cir. 1999) (citation omitted). The court looks first to intrinsic evidence, as "intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). Intrinsic evidence consists of the "patent itself, including the claims, the specification and, if in evidence, the prosecution history." Id. (citing Markman, 52 F.3d at 979). In the case at bar, there is no need to go beyond the intrinsic evidence of record, which includes the prosecution history, to construe the claims of the '094 patent. Cf. Tr. at 8 (counsel stating that plaintiff relies only on intrinsic evidence), 39-40 (counsel stating that defendant believes that intrinsic evidence is sufficient to sustain the government's claim construction arguments).

"[T]he words of a claim are generally given their ordinary and customary meaning." Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (internal quotations and citations omitted). More precisely, "the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Id. at 1313 (citations omitted). "[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." Id.

"Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history." Vitronics, 90 F.3d at 1582 (citations omitted). Thus, this court must always "review the specification to determine whether the inventor has used any terms in a manner inconsistent with their ordinary meaning." Id. While the claim is read in light of the specification, the court must not "read[] limitations from the specification into the claim." Phillips, 415 F.3d at 1323. In addition, the prosecution history of the patent may also be examined to exclude interpretations disclaimed by the inventor during prosecution. Chimie v. PPG Indus., Inc., 402 F.3d 1371, 1384 (Fed. Cir. 2005) (citing ZMI Corp. v. Cardiac Resuscitator Corp., 844 F.2d 1576, 1580 (Fed. Cir. 1988); Vitronics, 90 F.3d at 1582-83 (citations omitted).

Whether a claim's preamble limits the claim or merely provides an introduction to the invention is a common dispute in claim construction. The United States Court of Appeals for the Federal Circuit has discerned a number of general rules governing the construction of terms contained in a claim preamble:

> In general, a preamble limits the [claimed] invention if it recites essential structure or steps, or if it is necessary to give life, meaning, and vitality to the claim. [A] claim preamble has the import that the claim as a whole suggests for it. In other words, when the claim drafter chooses to use both the preamble and the body to define the subject matter of the claimed invention, the invention so defined, and not some other, is the one the patent protects. When limitations in the body of the claim rely upon and derive antecedent basis from the preamble, then the preamble may act as a necessary component of the claimed invention. On the other hand, [i]f the body of the claim sets out the complete invention, then the language of the preamble may be superfluous.

Eaton Corp. v. Rockwell Int'l Corp., 323 F.3d 1332, 1339 (Fed. Cir. 2003) (internal quotations and citations omitted). The prosecution history of the patent, as well, may help the court to determine whether the language in the preamble

limits the claim. E.g., Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc., 98 F.3d 1563, 1573 (Fed. Cir. 1996) (citations omitted). Although much more could be said on the construction of a claim preamble, these general rules provide a satisfactory framework for the court's analysis of the claims in the '094 patent.

III. Analysis

A. Accelerated or Enhanced Means "At Least One Month Earlier"

The parties' first dispute in claim construction is quite straightforward. Plaintiff argues that the adjectives accelerated and enhanced both signify that a desired characteristic (or characteristics) appears "at least one month earlier" in the life span of the transgenic mouse. ECF No. 75 at 42-44. Defendant contends that the terms accelerated and enhanced do not signify that the desired characteristic appears at least one month earlier in the life span of the transgenic mouse, but simply signify that the desired characteristic occurs "earlier" in the life span of the transgenic mouse.[2] ECF No. 76 at 15-20. Plaintiff offers the correct construction of these two terms.

Plaintiff asserts that the '094 patent contains a definition of accelerated and enhanced that falls within the "patentee acting as his own lexicographer" line of cases. ECF No. 75 at 30-32, 42. The court must agree. One statement in the '094 patent's specification, in particular, strongly supports this construction of the terms accelerated and enhanced:

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[2] The government's position as to the meaning of the term enhanced is variable, where sometimes the term means "earlier," whereas at other times, the term means "more." Compare ECF No. 76 at 33-34, with ECF No. 84 at 11-12, with Tr. at 40-41. This lack of consistency in the government's interpretation of the term enhanced does not strengthen its claim construction arguments. The court notes, too, that the government's description of the position of its former co-defendant regarding the construction of the term enhanced also lacks consistency. Compare ECF No. 76 at 34 (stating that the former co-defendant did not agree with the government's construction of enhanced), with ECF No. 84 at 11 (stating that the former co-defendant agreed with the government's construction of enhanced).

> Where earlier or accelerated, it is meant that the observed phenotype is seen at least one month earlier in the lifespan than the phenotype in the parental strain or similarly for later appearance.[3]

ECF No. 76-1 at 7 ('094 patent 5:18-21). Thus, the adjective accelerated has been given the definition in the '094 patent of "at least one month earlier in the life span" of the transgenic mouse. Id.

Although the adjective enhanced is not directly defined in this same section of the specification of the '094 patent, the court notes that, in the claims where the term enhanced occurs, the parallel use of the terms accelerated and enhanced is striking. Claim 1 announces that the transgenic mouse will have "enhanced Alzheimer's Disease related amyloid accumulation in its brain" such that the "mouse develops accelerated deposition of Aβ in its brain." Id. at 11. Similarly, Claim 13 announces that the method for producing this transgenic mouse that has "enhanced Alzheimer's Disease related amyloid pathology" will ensure that the mouse "develops accelerated deposition of AD[4] in its brain." Id. at 12. As evidenced by the parallelism within Claims 1 and 13, enhanced and accelerated are used in the '094 patent claims as synonyms.

Because accelerated means "at least one month earlier in the life span" of the transgenic mouse, and because accelerated and enhanced are used as synonyms, the court finds that both accelerated and enhanced mean "at least one month earlier in the life span" of the transgenic mouse. This construction is consistent with the patent specification which places great emphasis on producing mouse models for AD research where the transgenic mice exhibit desired traits earlier in their life spans. See ECF No. 76-1 at 6 ('094 patent 3:57-67; 4:1-4), 8 ('094 patent 8:15-26). For these reasons, the court construes accelerated and enhanced to signify "at least one month earlier in the life span" of the transgenic mouse.

Defendant proffers a number of arguments against this construction, but none is sufficient to overcome the most reasonable reading of the text of the claims and specification of the '094 patent. First, the government argues that the definition of accelerated is of limited applicability because it only appears in the

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[3] For the purposes of this analysis, a phenotype may be considered to be a characteristic or set of characteristics present in a transgenic mouse. See Tr. at 8, 10-11, 30.

[4] The term "AD" is a likely typographic error in the'094 patent replacing "Aβ." Cf. ECF No. 69-1 at 6 (where neither party proposes that Claim 13 specifies an earlier deposition of Alzheimer's Disease, but instead both parties suggest that Claim 13 specifies an earlier deposition of amyloid plaque features (or beta-amyloid plaques).

Preferred Embodiment section of the '094 patent. ECF No. 76 at 18; ECF No. 84 at 7-8. Although the court agrees with defendant that it may be error to limit a claim in light of language found only in a preferred embodiment of the invention, e.g., Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 904-08 (Fed. Cir. 2004), the language in a preferred embodiment of a patent may limit a claim if the limiting language is consistent with the inventor's general description of the invention, e.g., Biogen, Inc. v. Berlex Labs., Inc., 318 F.3d 1132, 1139-40 (Fed. Cir. 2003) (citations omitted). Here, because the definition of accelerated, and, by extension, of enhanced, is of general applicability to the invention in the '094 patent, it is not error to utilize that definition which is found in the sole preferred embodiment described in the '094 patent.

The government's second argument makes a distinction between mice of the "parental strain," ECF No. 76-1 at 7, which are contrasted with the invented strain of transgenic mice in the Preferred Embodiment, and other groups of mice that are contrasted with the transgenic mice of the '094 patent in the language of Claims 1, 3, 7-8, 10-11, and 13. ECF No. 76 at 19-20; ECF No. 84 at 8. At oral argument, counsel for plaintiff took the position that the distinctions between non-transgenic mice, singly transgenic mice, and parental transgenic mice as comparators for the claimed doubly transgenic mice are distinctions without a difference. Tr. at 46-47, 55. Counsel for defendant argued that these distinctions between parental and non-parental mice must be accorded some significance. Id. at 53-54. The court agrees with plaintiff. When the descriptors accelerated and enhanced are construed, the comparative benefit of "at least one month earlier in the life span" of the transgenic mouse is of equal benefit no matter which comparison group is selected. The distinctions between non-transgenic mice, singly transgenic mice, and parental transgenic mice are of no consequence for the construction of the claim terms accelerated and enhanced.

Third, the government argues, more generally, that the cited definitional sentence containing the phrase "at least one month earlier in the life span" of the transgenic mouse is vague, unclear, and not rigorous enough to serve as a definition for the terms accelerated and enhanced. ECF No. 76 at 17-19; ECF No. 84 at 6-7. The court disagrees. This is not a case where a party urges the court to pluck one particular definition from a thicket of competing and confused definitions in the specification of a patent. Here, the term accelerated is precisely defined in the '094 patent only by the sentence cited by plaintiff, ECF No. 76-1 at 7 ('094 patent 5:18-21), and the terms accelerated and enhanced take their definition from this sentence. The language relied upon by plaintiff is clear and is not vague.

Fourth, the government suggests that its claim construction, one which equates accelerated with an unspecified "earlier" amount of time, is consistent with various expressions in the specification and also raises no risk of indefiniteness. ECF No. 76 at 16; ECF No. 84 at 9-10. Plaintiff strongly disagrees. ECF No. 75 at 43-44. Plaintiff urges the court to adopt its claim construction to preserve the validity of the '094 patent, and to avoid construing

accelerated and enhanced in a manner that renders the claims of the '094 patent indefinite. Id. at 44 (citing Whittaker Corp. v. UNR Indus., Inc., 911 F.2d 709, 712 (Fed. Cir. 1990)). The court does not believe that the rule set forth in Whittaker applies here. See 911 F.2d at 712 (stating that "claims are generally construed so as to sustain their validity, if possible") (citation omitted).

The rule that patent claims are generally construed to preserve their validity, if possible, is "a doctrine of limited utility." Phillips, 415 F.3d at 1328. It does not apply when the claim is unambiguous, nor does it apply when a claim "can be construed without the need to consider whether one possible construction would render the claim invalid while the other would not." Id. Here, the meaning of the claim terms accelerated and enhanced is not ambiguous.

However, the court recognizes that "broad and amorphous" claim terms, such as accelerated and enhanced, benefit from a close reading of the specification. See, e.g., Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc., 262 F.3d 1258, 1269-70 (Fed. Cir. 2001) (Bell Atlantic) (noting, in that case, that "the ordinary meaning of the non-technical term 'mode' is sufficiently broad and amorphous that the scope of the claim language can be reconciled only with recourse to the written description" (citing Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed. Cir. 1998))). Here, following the rule in Bell Atlantic, the court relies upon the specification to supply the definition of accelerated and enhanced; that definition renders the patent claims unambiguous. Thus, the court need not construe the '094 patent claims to preserve their validity. Phillips, 415 F.3d at 1328.

Alternatively, if the '094 patent claims could be considered to be ambiguous, the court would agree with plaintiff that the claims should be construed to preserve their validity. Under the government's proposed construction of accelerated and enhanced, ECF No. 84 at 9-12, the invention is likely indefinite because there are no objective boundaries to the terms of degree earlier, or more. See, e.g., Berkheimer v. HP Inc., 881 F.3d 1360, 1364 (Fed. Cir. 2018) ("Our case law is clear that the objective boundaries requirement applies to terms of degree."); Liberty Ammunition, Inc. v. United States, 835 F.3d 1388, 1395-96 (Fed. Cir. 2016) ("We especially take caution when presented with terms of degree following the Supreme Court's decision in Nautilus, Inc. v. Biosig Instruments, Inc., [134 S. Ct. 2120] (2014)"), cert. denied, 137 S. Ct. 1825 (2017). Thus, if the claims of the '094 patent could be deemed to be ambiguous in their use of the terms accelerated and enhanced, the court would adopt plaintiff's construction of these terms to preserve the claims' validity.

Finally, the government argues that plaintiff's proposed construction of the term enhanced is flawed, because no sufficient definition of this term in the specification of the '094 patent displaces the ordinary meaning of the term enhanced. ECF No. 76 at 34; ECF No. 84 at 11-12. In the same vein, the government also relies on a discussion of the term enhanced during the prosecution history of the '094 patent. ECF No. 84 at 12. Beyond these two

arguments that rely on intrinsic evidence, the government relies, in addition, on a dictionary definition of the verb "enhance" to suggest that the definitions "more," "raise[d]" or increase[d]" capture the meaning of the term enhanced in the claims of the '094 patent. Id. at 12; see also ECF No. 76 at 34; Tr. at 41.

Plaintiff argues, and the court has found, that the specification provides a definition for accelerated and enhanced so that in the claims of the '094 patent, enhanced means "at least one month earlier in the life span" of the transgenic mouse. ECF No. 75 at 30-32. According to plaintiff,

> [t]here is nothing in the Specification, nothing in the Prosecution History or any other aspect of the intrinsic evidence that suggests [that] the term "accelerated" or "enhanced" can mean anything but at least one month earlier in the lifespan of the mouse.

Id. at 31. The court agrees with plaintiff that enhanced, as used in Claims 1 and 13, must be construed to indicate that the desired trait (or traits) occurs at least one month earlier in the life span of the transgenic mouse.

In the court's view, the extrinsic evidence of the dictionary definition of the verb "enhance" does not outweigh the specification language relied upon by plaintiff, and the parallel use of accelerated and enhanced in Claims 1 and 13. See supra. Further, the unenlightening discussion of the term enhanced which took place during the prosecution history of the '094 patent, one which referenced, in the government's words, "generic terminology in the prior art," ECF No. 84 at 12, also does not replace the clear definition of the term enhanced provided by the specification and by the parallel use of the terms accelerated and enhanced in Claims 1 and 13. Ambiguous statements in the prosecution history should be accorded less weight than the specification language of the patent itself. See, e.g., Phillips, 415 F.3d at 1317 ("[B]ecause the prosecution history represents an ongoing negotiation between the [United States Patent and Trademark Office (PTO)] and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes.") (citations omitted). Having considered all of defendant's arguments as to the construction of the term enhanced in Claims 1 and 13, including those that rely on extrinsic evidence, not just intrinsic evidence, the court concludes that plaintiff's construction of the term enhanced is correct.[5]

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[5] Defendant also contends that because the word enhanced appears along with the word accelerated in some sentences within the specification, this phenomenon supports the government's construction of the term enhanced. ECF No. 84 at 12 (citing '094 patent 4:3-4; 4:9). As plaintiff's counsel noted at oral argument, however, the paramount concern of timing in the '094 patent supports plaintiff's construction of the term enhanced in Claims 1 and 13, i.e., that

B. Alzheimer's Disease Related Pathology

The second claim construction dispute in this case is also straightforward. Plaintiff contends that any mention in the claims of the '094 patent of Alzheimer's Disease related pathology, or some variant of that phrase, necessarily refers to a constellation of three markers for AD pathology, wherein the transgenic mice manifest: (1) fibrillary deposits of Aß; (2) reactive gliosis; and, (3) a loss of spontaneous alternation behavior. ECF No. 75 at 53. Defendant, on the other hand, urges construction of the term Alzheimer's Disease related pathology -- should the court decide that this language limits any claim in the '094 patent -- to mean "having a characteristic of Alzheimer's disease (e.g., beta-amyloid plaques)." ECF No. 76 at 22, 32-33. In the court's view, defendant's construction of this term hits closer to the mark.

Plaintiff's proposed construction depends on two foundational premises, both of which are fundamentally flawed.[6] The first premise is that the applicants acted as their own lexicographer, before the PTO, to substitute a special definition for Alzheimer's Disease related pathology that displaces the ordinary and customary meaning of this term. ECF No. 75 at 10, 45-46; ECF No. 83 at 34-35, 41; Tr. at 16-19. The second premise is that the specification of the '094 patent clearly sets forth a definition for Alzheimer's Disease related pathology that requires that all three traits -- fibrillary deposits of Aß; reactive gliosis, and the loss of spontaneous alternation behavior -- occur in the claimed doubly transgenic mouse. ECF No. 75 at 32-34, 45; ECF No. 83 at 29-32, 40; Tr. at 13-16, 20, 44-45, 55. Neither of these premises is supported by the intrinsic evidence before the court.

1. Prosecution History Evidence

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enhanced means "at least one month earlier in the life span" of the transgenic mouse. Tr. at 51.

[6] Plaintiff's proposed claim construction also suffers from an inconsistency. Plaintiff argues, on one hand, that when a specific AD related pathology is cited in a claim, this specific reference shows that the claim does not require that the claimed mouse display all three desirable traits. See ECF No. 75 at 46 n.6. On the other hand, in its proposed claim constructions, plaintiff specifically proposes a construction which states that the mice described in Claims 8 and 9 must display all three desirable traits, notwithstanding the claim language in Claims 8 and 9 citing one specific AD related pathology. ECF No. 69-1 at 8; ECF No. 75 at 58-59. These statements advance fundamentally inconsistent and contradictory claim construction positions.

Plaintiff acknowledges that its reliance on prosecution history is somewhat distinctive, in that the lexicographer who purportedly replaced the plain meaning of Alzheimer's Disease related pathology with a specialized definition was the patent examiner, not the applicant. Tr. at 19. "The crafter of the claims, which is often the applicant, but in this case was the Examiner, as a result of discussion and exchange between the two in prosecution, formulated a specific definition that applicants attempted to embrace and the Examiner wrote for them." Id. While the court does not categorically reject plaintiff's theory that a patent examiner may, in certain circumstances, assist the applicant in lexicography, here there is no evidence that the applicants rewrote the patent to incorporate any specific definition of Alzheimer's Disease related pathology provided by the patent examiner, or that they manifested any type of assent to the definition that might have been proposed by the patent examiner. Indeed, as defendant argues, the prosecution history of the '094 patent shows that the applicants did not expressly adopt the definition allegedly proposed by the patent examiner, and that the applicants may have, instead, rejected the examiner's proposed formulation. ECF No. 84 at 21-24.

The court has carefully examined the exhibits attached to the parties' claim construction briefs relevant to the dialogue between the applicants and the patent examiner. See ECF Nos. 75-2; 75-3; 75-4; 76-2. While it is true that the patent examiner noted, on March 12, 1998, that three characteristics of AD were implicated by traits obtained in the claimed doubly transgenic mice, see ECF No. 75-2 at 3-5, 7, these comments by the examiner did not elicit any affirmative amendments to the patent reproducing the language employed by the examiner, nor did the applicants acknowledge that the examiner had provided the specialized definition that would govern the interpretation of the term Alzheimer's Disease related pathology in the '094 patent. Indeed, on June 15, 1998, the applicants, instead, referenced "increased levels of amyloidogenic Aß" as the "enhanced AD phenotype" obtained in the claimed mice. ECF No. 75-3 at 19. In other statements communicated to the patent examiner on June 15, 1998, the applicants noted that the "[t]he amyloid pathology is generally increased levels of amyloidogenic Aß," and that the claimed mice show "accelerated amyloid deposition." Id. at 14-15. On this record, a person of ordinary skill in the art was not aware from the prosecution history of the '094 patent that the applicants had adopted a specialized definition of the term Alzheimer's Disease related pathology that originated with the patent examiner.

To the extent that plaintiff asserts that its prosecution history analysis is on all fours with any of the caselaw cited in plaintiff's briefs or at oral argument, see ECF No. 75 at 50; Tr. at 8, the court disagrees. In Biogen Idec, Inc. v. GlaxoSmithKline LLC, 713 F.3d 1090, 1093-94, 96-97 & n.6 (Fed. Cir. 2013), for example, the district court adopted a claim construction based on the applicant's explicit acknowledgement of a limitation proposed by the patent examiner, and the Federal Circuit affirmed on this ground. Similarly, in Aptalis Pharmatech, Inc. v. Apotex Inc., No. 2017-1344, 2018 WL 286123, at *4-5 (Fed. Cir. Jan. 4, 2018), an unpublished decision cited by plaintiff, the Federal Circuit found support for the

appellants' claim construction position in the language of a declaration submitted by the applicants during the prosecution of the patent, which summarized a dialogue between the patent examiner and an expert in the field of the invention. In these cases cited by plaintiff, the defining language was submitted or acknowledged by the applicant in the course of prosecution. In this case, in contrast, plaintiff attempts to leverage a statement of the patent examiner, one that is unaccompanied by any acknowledgment or adoption on the part of the applicants, to support plaintiff's proposed claim construction.

Neither the intrinsic evidence of the prosecution history, nor the caselaw relied upon by plaintiff, supports plaintiff's proposed claim construction. The court concludes that the prosecution history of the '094 patent does not support plaintiff's proposed construction of the term Alzheimer's Disease related pathology. The court now turns to plaintiff's arguments based on the specification of the '094 patent.

2. Specification Language

At oral argument, the court asked plaintiff's counsel to identify "more specific cites" to the specification that support plaintiff's proposed construction of the term Alzheimer's Disease related pathology. Tr. at 14. To answer the court's question, counsel pointed to Columns 5-8 of the '094 patent, as well as to Columns 9-11. Id. at 14-16. According to the court's calculation, the definition for Alzheimer's Disease related pathology, as related by plaintiff, must be distilled from more than four hundred lines of text of the patent specification, encompassing the entirety of the "Detailed Description of the Preferred Embodiment," as well as almost the entirety of the "Examples" section. See ECF No. 76-1 at 7-10. There is no summarizing sentence or paragraph in this wide swath of text that provides the three-component specialized definition that plaintiff urges the court to adopt. Nor, as defendant points out, does the term "reactive gliosis," which is part of plaintiff's definition of the contested term Alzheimer's Disease related pathology, appear anywhere in the '094 patent.[7] See ECF No. 84 at 15 n.12. Thus, plaintiff's effort to convince the court that its proposed definition for "Alzheimer's Disease related pathology" is "clearly stated" in the specification is completely at odds with the text of the specification. Vitronics, 90 F.3d at 1582.

Plaintiff notes, nonetheless, that the "patent Specification considers the fibrillary amyloid deposits in the brain, reactive gliosis and loss of spontaneous alternation behavior." ECF No. 75 at 45 (citing '094 patent 10:22 to 11:37). This is a plausible reading of the specification, but the extended discussion in the specification of these three desired traits in the claimed mice is unmoored from

[7] Plaintiff's counsel was therefore imprecise when he stated that "the loss of nerve cells, astrocytes, [was] generally referred to as reactive gliosis in the patent." Tr. at 13.

any definitional statement that all three of these characteristics must be present for the phrase Alzheimer's Disease related pathology to have meaning. Plaintiff thus invites the court to improperly import a limitation from the specification into the claims, when the court must, instead, read the claims in light of the specification. Phillips, 415 F.3d at 1323.

In its reply brief, plaintiff urges the court to consider the penultimate paragraph of the Preferred Embodiment section of the '094 patent, which contains a summary, of a sort, of the advantages of the claimed mice. ECF No. 83 at 29-30. The cited text is as follows:

> These results clearly demonstrate that presenilin mutations accelerate development of the AD phenotype in K670N,M671L mice in a synergistic manner and provides a modulated phenotype. The data indicate that mutant presenilin affects the processing of mutant APP expressed from the K670N,MG71L transgene to enhance Aß production, fibrillar plaque formation and affect behavior early in the life-spans of mice. The rapid development of the AD phenotype in these mice will be advantageous in addressing mechanistic issues of amyloid toxicity, and testing the efficacy of agents proposed to interact with select aspects of the AD phenotype.

ECF No. 76-1 at 8 ('094 patent 8:15-26). This section of the patent does not aid plaintiff. Any three-component definition of the term Alzheimer's Disease related pathology that could be derived from this paragraph is captured in the phrase "to enhance Aß production, fibrillar plaque formation and affect behavior early in the life-spans of mice." Id. The three components of any such definition do not include reactive gliosis or any mention of astrocytes, and any such definition doubles the emphasis on Aß production and fibrillar Aß deposits/plaques. Again, the text of the specification contains no support for plaintiff's proposed three-component definition of the term Alzheimer's Disease related pathology.

The court has considered all of the parties' arguments based on the specification and the language and structure of the claims which contain the term Alzheimer's Disease related pathology. None of these arguments convince the court that the specification contains the three-component specialized definition of that term proposed by plaintiff. The court therefore turns to defendant's proposed construction of this term.

Defendant argues that the correct construction of the term Alzheimer's Disease related pathology is "having a characteristic of Alzheimer's disease (e.g., beta-amyloid plaques)." ECF No. 69-1 at 4-5; ECF No. 76 at 22. Plaintiff, somewhat incongruously, finds the use of the word "plaques" in defendant's construction to be inappropriate, on the grounds that the word "plaque" is "nowhere substantively employed" in the '094 patent. ECF No. 75 at 47. As defendant notes, plaintiff's resistance to the use of the word "plaques" is undermined by plaintiff's use of the phrase "plaque features" in one of its

proposed constructions of the term Alzheimer's Disease related pathology. See ECF No. 69-1 at 4-8; ECF No. 84 at 15 n.12.

The court notes, too, that the word "plaque" is mentioned several times in the '094 patent -- in the titles of prior art publications, in the Background of the Invention section, in the Preferred Embodiment section, in the Examples section, and in a table of test results comparing the claimed mice to singly transgenic mice. ECF No. 76-1 at 3, 5, 8-11. The patentee appears to have made substantive employment of the word "plaque."[8] Defendant suggests, in any case, that the court might substitute the word "deposition" for "plaques," in defendant's proposed construction, to address plaintiff's concern. See ECF No. 84 at 15 n.12. Indeed, in the court's view, if the occurrence of the words "deposits" or "deposition" is tracked throughout the '094 patent, this formulation is more common than the substantive use of the word "plaque."

Having considered the almost innumerable variations in the description of amyloid deposits in the mouse brain that are contained in the '094 patent, the court believes that the "formation of deposits containing Aß in the brain" captures this concept. See, e.g., ECF No. 76-1 at 8 ('094 patent 7:57-58), 9 ('094 patent 9:63), 10 ('094 patent 11:9). Thus the court slightly alters defendant's proposed construction, and construes the term Alzheimer's Disease related pathology in the following manner: "having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain." This formulation is in accordance with the language of the specification, and also is in accordance with the phrasing of the invention in a great number of the claims, where the claimed mouse or mice "develop[s] . . . deposition of Aß in its [or their] brain[s]." ECF No. 76-1 at 11-12 (Claims 1, 3, 5, 7, 10, 13).[9]

Plaintiff invokes the claim differentiation doctrine in an effort to convince the court that defendant's proposed claim construction of the term Alzheimer's Disease related pathology is infirm. ECF No. 75 at 11-12, 47-48; ECF No. 83 at 36-37; Tr. at 20. Plaintiff argues that if the term Alzheimer's Disease related pathology means "having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain," this term is too similar to the term "accelerated or enhanced deposition of Aß in the brain," another term of art found in many of the claims of the '094 patent. The court does not agree.

The preambles of the claims contain the term Alzheimer's Disease related pathology, which refers to any one of the characteristics of Alzheimer's Disease,

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[8] At least as compared to plaintiff's proposed use of the term "reactive gliosis," which is nowhere employed in the '094 patent, the word "plaque" is substantively employed in the patent.

[9] Correcting for a likely typographic error in Claim 13, substituting Aß for AD. See supra note 4.

such as the formation of deposits containing Aß in the brain, whereas the body of the claim specifically notes that accelerated or enhanced deposition of Aß occurs in the brains of the claimed mice. Although these terms are similar, they are easily distinguished. The court notes, too, that the claim differentiation doctrine is merely a rule of thumb that does not trump clear indicators of meaning found in the specification. E.g., Edwards Lifesciences LLC v. Cook Inc., 582 F.3d 1322, 1332 (Fed. Cir. 2009) (citing Netcraft Corp. v. eBay, Inc., 549 F.3d 1394, 1400 n.1 (Fed. Cir. 2008)). Even if defendant's construction of the term Alzheimer's Disease related pathology offended the doctrine of claim differentiation, which it does not, that doctrine would not outweigh the language of the specification -- and of the claims themselves -- which provides the proper construction of this term.

Further, the prosecution history of the '094 patent clearly identifies five characteristics of Alzheimer's Disease that would be useful in transgenic mice: fibrillar Aß deposits, reactive gliosis, increased maze activity, neurofibrillary tangles, and massive neuronal loss. ECF No. 75-2 at 5. The court's construction of the term Alzheimer's Disease related pathology takes this fact into account by stating that "having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain," is a feature of the invention in the '094 patent. The court's construction of the disputed term reflects both the prosecution history and the specification of the '094 patent, and allays any concern that this term is not sufficiently differentiated from other terms in the claims of the '094 patent which focus solely on Aß accumulation or deposits.[10]

Thus, the court adopts a slightly modified form of defendant's proposed construction. The term Alzheimer's Disease related pathology in the claims of the '094 patent means "having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain." The court now turns to the parties' final dispute, where plaintiff and defendant disagree as to whether the claims' preambles limit the claims of the '094 patent.

C. Preamble Language

There are two facets to this dispute. First, plaintiff appears to suggest that the court should not decide, during the Markman phase of this litigation, whether the language of the claim preambles limits the claims. See Tr. at 19 ("This is not

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[10] The court must disagree with defendant that the word "pathology" excludes cognitive deficits associated with Alzheimer's Disease. Cf. Tr. at 39. The text of the specification relied upon by defendant is ambiguous, see ECF No. 76-1 at 6 ('094 patent 3:3-8), and runs counter to the discussion of AD pathology in the prosecution history, see ECF No. 75-2 at 5. Because the intrinsic evidence is sufficient to show that cognitive impairments are encompassed in the term pathology in the '094 patent, the court need not turn to extrinsic evidence to construe the word pathology.

the time, we submit, that you determine whether the preamble is limiting or not, although the parties have discussed [this issue] in their briefs."), 48 ("Our view of the case law says this is not the time [to determine whether a preamble limits a claim]."). Second, if the question is properly before the court at this time, plaintiff suggests that the preamble language is limiting, whereas defendant argues that the preamble language of the '094 patent claims is not limiting. The court addresses each of these questions in turn.

1. Determining Whether the Preamble Is Limiting Is Part of Claim Construction

Plaintiff's hypothesis, that claim construction does not include a determination of whether a preamble limits a claim, was not clearly presented until oral argument, although a vague precursor of this hypothesis was presented in plaintiff's reply brief.[11] As such, plaintiff's argument is not properly before the court. See, e.g., Novosteel SA v. United States, 284 F.3d 1261, 1274 (Fed. Cir. 2002) (finding that a party waived an argument that was first presented to the trial judge in a reply brief); Cubic Def. Sys., Inc. v. United States, 45 Fed. Cl. 450, 467 (1999) (finding that a party waived arguments presented for the first time at oral argument). Nor was plaintiff's contention at oral argument supported by any citation to caselaw.[12] Even so, plaintiff's hypothesis is quickly rebutted by reference to any number of decisions of the Federal Circuit, where that court addressed the status of a claim preamble, as limiting or not limiting, in the context of claim construction. See, e.g., Pacing Techs., LLC v. Garmin Int'l, Inc., 778 F.3d 1021, 1023 (Fed. Cir. 2015) (noting that the claim construction dispute in that case "turn[ed] on whether the preamble to claim 25 is limiting and on the construction of a 'repetitive motion pacing system' as recited in the preamble"); Bicon, Inc. v. Straumann Co., 441 F.3d 945, 952 (Fed. Cir. 2006) (considering an appellant's arguments concerning "the role of preamble language in claim construction" and finding that certain preamble language limited the claim); Schumer v. Lab. Comput. Sys., Inc., 308 F.3d 1304, 1310 (Fed. Cir. 2002) (finding error in a district court's claim construction because that construction mistakenly found that the preambles limited the claims); Bell Commc'ns Research, Inc. v. Vitalink Commc'ns Corp., 55 F.3d 615, 621 (Fed. Cir. 1995) (Bell Communications) ("Preamble construction thus presents no deeper mystery than the broader task of claim construction, of which it is but a part.").

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[11] Plaintiff stated in its reply brief that "claim terms are construed on the basis of the patent's file history, not whether they are 'limiting' or not." ECF No. 83 at 26.

[12] Indeed, plaintiff's initial claim construction brief suggested that this is the time for the court to decide whether language in the preambles is limiting on the claims of the '094 patent, because that very topic was addressed at some length. ECF No. 75 at 12-15.

The correct approach to preambles and the claim limitation issue is supplied, in part, in Schumer. Language in a claim preamble is of no significance to claim construction where the preamble does not limit the claim. Schumer, 308 F.3d at 1310 (citing Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1373-74 (Fed. Cir. 2001)). In such a situation, the preamble language is superfluous. Id. (citing Manning v. Paradis, 296 F.3d 1098, 1103 (Fed. Cir. 2002)). Where, however, a preamble may limit a claim, the court may need to construe terms contained in the preamble, and determine whether the preamble is limiting, to construe the claims of the patent. See, e.g., Seachange Int'l, Inc. v. C-COR, Inc., 413 F.3d 1361, 1375-77 (Fed. Cir. 2005) (construing terms in a preamble and finding that the preamble was limiting); Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 811 (Fed. Cir. 2002) (construing a term in both a preamble and the body of the claim and deciding that the preamble was limiting). Thus, in this case, the court has first construed the disputed terms in the claim preambles, and now must determine whether the preamble language limits the claims in the '094 patent to complete its claim construction task.[13]

2. The Preamble Language Is Limiting in This Case

Many of the preamble construction guidelines cited by the parties are of potential relevance to the question of whether the claim preambles of the '094 patent are limiting. Unfortunately, these guidelines can prove to be ambiguous and produce widely varying results at the trial level and upon appeal. For example, simply because a preamble appears to contain an "antecedent basis" for a term mentioned in the body of a claim is no guarantee that the preamble is limiting. See Eaton, 323 F.3d at 1339 ("When limitations in the body of the claim rely upon and derive antecedent basis from the preamble, then the preamble may act as a necessary component of the claimed invention.") (emphasis added) (citations omitted). The preamble language must still supply some additional, vital information that is missing from the body of the claim for that particular guideline to apply. See, e.g., TomTom, Inc. v. Adolph, 790 F.3d 1315, 1322-24 (Fed. Cir. 2015) (ruling that certain preamble terms were not limiting because these terms were merely duplicative of the terms in the body of the claim, even though the preamble did provide an antecedent basis for another term in the body of the claim) (citations omitted); Am. Med. Sys., Inc. v. Biolitec, Inc., 618 F.3d 1354, 1359 (Fed. Cir. 2010) ("We have held that the preamble has no separate

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[13] In this particular case, it would have been difficult to determine whether the preamble language limits the claims in the '094 patent without first construing the disputed terms within the preambles. Another approach would be to first determine whether the preamble contains a claim limitation. See, e.g., Symantec Corp. v. Comput. Assocs. Int'l, Inc., 522 F.3d 1279, 1288 (Fed. Cir. 2008) ("Because the disputed term appears in the preamble to claim 1, we must first determine whether it is in fact a separate [claim] limitation."). In the instant case, the end result would necessarily be the same.

limiting effect if, for example, 'the preamble merely gives a descriptive name to the set of limitations in the body of the claim that completely set forth the invention.'" (quoting IMS Tech., Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434-35 (Fed. Cir. 2000))).

The court relies, therefore, on one particular guideline that, under the facts of this case, is dispositive for the construction of the claims in the '094 patent:

> [C]lear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention.

Catalina, 289 F.3d at 808-09 (citation omitted). When such evidence is found in the prosecution history of the patent, the drafter has chosen "to use both the preamble and the body to define the subject matter of the claimed invention, [and] the invention so defined, and not some other, is the one the patent protects." Bell Communications, 55 F.3d at 620 (citations omitted). Because the drafting of each of the claims of the '094 patent shows an intent to use the preamble to distinguish the claimed invention from the prior art, the preamble terms limit the claims.

Both parties in this litigation have acknowledged that the patent examiner's concerns about the initial version of the '094 patent led to extensive revisions of the language of the claims in the '094 patent. ECF No. 75 at 38; ECF No. 84 at 20-21. The record shows, and defendant acknowledges, that substantive changes were made to the claim preambles to address the examiner's concerns. ECF No. 76-2 at 44-50; ECF No. 76-6 at 2-7; ECF No. 84 at 20-21. According to plaintiff's counsel, a key term in the claim preambles was "coined" by the examiner and "embraced" by the applicants. Tr. at 19. Having studied the prosecution history and the parties' interpretation of that history, the court concludes that the claim preambles were designed to distinguish the claimed invention from the prior art and to ensure that other concerns, such as enablement, were addressed. This history satisfies, in the court's view, the requirement for a "clear reliance on the preamble during prosecution." Catalina, 289 F.3d at 808-09 (citation omitted).

In this context, the variation in the preambles among the claims in the '094 patent has little significance for the inquiry into whether these preambles contain claim limitations. The prosecution history of the '094 patent shows that both the preamble and the body of each claim functioned as coordinated expressions of the invention. Bell Communications, 55 F.3d at 620 (citations omitted). The court has considered all of defendant's arguments to the contrary but finds that these

arguments ignore the impact of the patent examiner's extensive restructuring and rewriting of the claims in the '094 patent.[14]

Finally, even if the court were to ignore the prosecution history of this patent, which it should not, defendant's attack on the preambles is based largely on defendant's assertion that the preambles are superfluous. ECF 76 at 21-22; ECF No. 84 at 13. They are not. The claim preambles that include the disputed term Alzheimer's Disease related pathology, for example, namely the preambles of Claims 3, 5, and 7, cannot be considered to be superfluous. This disputed term, as construed here by the court, introduces a broader definition of AD related characteristics than otherwise is present in each of these claims. The preamble states that an AD related characteristic, which might or might not be the specific example of the "formation of deposits containing Aß in the brain," is accelerated in the claimed mouse. That is not a superfluous statement of a claim limitation.

For the above reasons, the court finds that the preambles of the '094 patent are limiting and that the disputed terms within those preambles must be construed as part of the claim construction task before the court. Catalina, 289 F.3d at 808-09.

IV. Conclusion

The court sets forth its construction of disputed claim terms in the table that is attached to this order (Attachment 1). The court construes accelerated and enhanced to signify "at least one month earlier in the life span" of the transgenic mouse. The term Alzheimer's Disease related pathology means "having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain." The table also includes the parties' joint constructions of claim terms proposed in the Joint Claim Construction Chart, ECF No. 69-1 at 3. In addition, certain minor irregularities in proposed claim construction language for which the resolution was self-evident in light of the actual text of the claims, the parties' filings, their presentations at oral argument, and the analysis contained in this order, are also included within this table.[15]

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[14] This rewriting of the claims fundamentally altered their text, as evidenced by a serious flaw in Claims 4 and 6 -- those claims did not survive the rewriting process with any logical coherence. See ECF No. 75 at 38 n.5.

[15] Plaintiff's positions on claim construction are inconsistent, as shown by a comparison of the Joint Claim Construction Chart, ECF No. 69-1, and its initial brief, ECF No. 75 at 51-53, 55-62. The court has reconciled the inconsistencies by relying on both proposed constructions proffered by plaintiff. In addition, the court confirmed with plaintiff's counsel at oral argument that the joint constructions contained in the Joint Claim Construction Chart were acceptable to plaintiff. Tr. at 43. Finally, as to Claim 13's preamble, the court finds that no construction is needed for the term "Alzheimer's Disease related amyloid

IT IS SO ORDERED.

s/ Patricia E. Campbell-Smith
PATRICIA E. CAMPBELL-SMITH
Judge

pathology," as is the case for the term "Alzheimer's Disease related amyloid accumulation" in Claim 1's preamble.

ATTACHMENT 1: CLAIM CONSTRUCTION TABLE

Claim #	Passage to be Construed	Construction
#1 Preamble	A transgenic mouse with "enhanced Alzheimer's Disease related amyloid accumulation" in its brain	A transgenic mouse with Alzheimer's Disease related amyloid accumulation in its brain at least one month earlier in its life span than a mouse expressing one or no transgenes
#1 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#1 Body	mouse develops "accelerated deposition of Aß" in its brain as compared to non-transgenic mice or either parental mouse	mouse develops deposition of Aß in its brain at least one month earlier in the mouse's life span as compared to non-transgenic mice or either parental mouse
#3 Preamble	A transgenic mouse with "accelerated Alzheimer's Disease related pathology"	A transgenic mouse having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain, that occurs at least one month earlier in the mouse's life span than in a corresponding mouse expressing only one or none of the transgenes
#3 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#3 Body	mouse develops "accelerated deposition of Aß" in their brains as compared to non-transgenic mice or transgenic mice expressing either transgene	mouse develops deposition of Aß in their brains at least one month earlier in the mouse's life span as compared to non-transgenic mice or transgenic mice expressing either transgene

#5 Preamble	A transgenic mouse with "accelerated Alzheimer's Disease related pathology"	A transgenic mouse having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain, that occurs at least one month earlier in the mouse's life span than in a corresponding mouse expressing only one or none of the transgenes
#5 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#5 Body	"mouse develops accelerated deposition of Aß in its brain within six months of birth as compared to non-transgenic mice or transgenic mice expressing either transgene"	mouse has increased deposition of Aß in its brain by its sixth month of life as compared to deposits typically found in non-transgenic mice or as compared to deposits typically found in transgenic mice expressing either transgene
#7 Preamble	A transgenic mouse with "accelerated Alzheimer's Disease related pathology"	A transgenic mouse having a characteristic of Alzheimer's Disease, such as the formation of deposits containing Aß in the brain, that occurs at least one month earlier in the mouse's life span than in a corresponding mouse expressing only one or none of the transgenes
#7 Body	"DNA sequence encoding mutant presenilin"	any DNA sequence that, if made part of a mouse genome, can be caused to express a mutant form of a presenilin protein
#7 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse

#7 Body	"accelerated pathology develop"	mouse develops (appears to be a typographic error, compare Claims 5, 8, 10, 11)
#7 Body	"accelerated deposition of Aß" in its brain as compared to non-transgenic mice or transgenic mice expressing either transgene	deposition of Aß in its brain at least one month earlier in the mouse's life span as compared to non-transgenic mice or transgenic mice expressing either transgene
#8 Preamble	"elevated levels of amyloidogenic Aß (Aß42(43)) as a pathology for Alzheimer's Disease"	No construction needed
#8 Body	"DNA sequence encoding mutant presenilin"	any DNA sequence that, if made part of a mouse genome, can be caused to express a mutant form of a presenilin protein
#8 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#8 Body	mouse develops "accelerated deposition of Aß (Aß42(43))" in its brain as compared to non-transgenic mice or transgenic mice expressing either transgene	mouse develops deposition of Aß (Aß42(43)) in its brain at least one month earlier in the mouse's life span as compared to non-transgenic mice or transgenic mice expressing either transgene
#9 Preamble	"elevated levels of amyloidogenic Aß (Aß42(43)) as a pathology for Alzheimer's Disease"	No construction needed
#9 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse

#10 Body	"DNA sequence encoding mutant presenilin"	any DNA sequence that, if made part of a mouse genome, can be caused to express a mutant form of a presenilin protein
#10 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#10 Body	mouse develops "accelerated deposition of Aß" in its brain as compared to non-transgenic mice or either parental mouse	mouse develops deposition of Aß in its brain at least one month earlier in the mouse's life span as compared to non-transgenic mice or either parental mouse
#11 Preamble	"elevated levels of amyloidogenic Aß (Aß42(43)) as a pathology for Alzheimer's Disease"	No construction needed
#11 Body	"DNA sequence encoding mutant presenilin"	any DNA sequence that, if made part of a mouse genome, can be caused to express a mutant form of a presenilin protein
#11 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#11 Body	mouse develops "accelerated deposition of Aß (Aß42(43))" in their brains as compared to non-transgenic mice or either parental mouse	mouse develops deposition of Aß (Aß42(43)) in their brains at least one month earlier in the mouse's life span as compared to non-transgenic mice or either parental mouse

#13 Preamble	a transgenic mouse with "enhanced Alzheimer's Disease related amyloid pathology"	a transgenic mouse with Alzheimer's Disease related amyloid pathology that occurs at least one month earlier in the mouse's life span than a corresponding mouse expressing only one or none of the transgenes
#13 Body	"operably linked to a promoter"	linked to a promoter sequence, which allows the transgene to be expressed by the mouse
#13 Body	mouse develops "accelerated deposition of AD" in its brain as compared to non-transgenic mice or either parental mouse	mouse develops deposition of Aß in its brain at least one month earlier in the mouse's life span as compared to non-transgenic mice or either parental mouse