UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

MEDICINOVA, INC., a Delaware Corporation, Plaintiff, v. GENZYME CORPORATION, a Massachusetts Corporation, Defendant.	Case No.: 14-CV-2513 JLS (KSC) **ORDER ON CLAIM CONSTRUCTION AND DENYING PLAINTIFF'S MOTION TO STRIKE** (ECF Nos. 123, 126, 130)

Presently before the Court are Plaintiff MediciNova, Inc.'s ("Pl.'s Br.," ECF No. 126) and Defendant Genzyme Corporation's ("Def.'s Br.," ECF No. 123) Opening Claim Construction Briefs, as well as each Party's response to the other's Opening Claim Construction Brief ("Def.'s Resp.," ECF No. 134; "Pl.'s Resp.," ECF No. 135). The Parties dispute the construction of a single term—"a stock of recombinant adeno-associated virus"—claimed by U.S. Patent No. 6,376,237 (the "'237 patent"). Also before the Court is Plaintiff's Motion to Strike Portion's of Genzyme Corporation's Opening Claim Construction Brief ("Mot. to Strike," ECF No. 130), as well as Defendant's Opposition ("Opp'n," ECF No. 132).

The Court heard oral argument, including tutorials from the Parties' respective experts, on June 18, 2019. *See* ECF No. 144. Having carefully considered the Parties'

arguments, the evidence, and the law, the Court **DENIES** the Motion to Strike and **ADOPTS** Genzyme's proposed construction.

BACKGROUND

I. Factual Background

A. The '237 Patent

Through gene therapy, physicians aim "to treat disease by infecting a patient's body with genetic material designed to produce therapeutic material that treats the disease." Declaration of M. Curt Lambert in Support of Def.'s Br. ("Lambert Decl.") Ex. K at 504.[1] There are various ways to introduce this therapeutic genetic material, sometimes referred to as a "heterologous gene," *see* Lambert Decl. Ex. A ("'237 patent") at 9:3–20, into a patient's body, one of which involves the use of recombinant viruses. '237 patent at 2:1–7. A recombinant virus is "a virus that has been genetically altered, e.g., by the addition or insertion of a heterologous nucleic acid construct into the particle." '237 patent at 8:12–14.

One means of viral-mediated gene delivery is the use of adeno-associated virus ("AAV") vectors. '237 patent at 2:7–9, 15–16. There are various benefits to using AAV as compared to other viruses. '237 patent at 2:17–18. For example, AAV can "infect a wide range of host cells, including non-dividing cells," can "infect cells from different species," "has not been associated with any human or animal disease[,] and does not appear to alter the biological properties of the host cell upon integration." '237 patent at 2:18–23. Further, AAV is "stable at a wide range of physical and chemical conditions." '237 patent at 2:26–27.

AAV contains a single-stranded deoxyribonucleic acid ("DNA") molecule. '237 patent at 2:28–29. The AAV genome comprises an internal, non-repeating genome that is flanked on either end by inverted terminal repeats ("ITRs"). '237 patent at 2:29–31. The

[1] In citing to Defendant's supporting materials, except for deposition transcripts, the Court cites to the consecutive pagination provided by Defendant and stamped at the bottom of each page.

non-repeating genome is itself comprised of AAV replication ("rep") and capsid ("cap") genes, which code for viral proteins allowing the virus to replicate and package, respectively, its viral genome into a virion. '237 patent at 2:36–40. AAV may be engineered to deliver a therapeutic heterologous gene by deleting the internal, non-repeating portion of the AAV genome, *i.e.*, the rep and cap genes, and inserting the heterologous gene between the two ITRs. '237 patent at 2:59–62. This is referred to as an AAV vector. *See* '237 patent at 6:64–7:10.

To produce an infectious recombinant AAV (or "rAAV") containing the heterologous gene, the AAV vector and two other components must be introduced to a suitable host cell. *See* '237 patent at 3:1–10. One of these additional components is a vector, called the "AAV helper construct," *see* '237 patent at 7:22–40, that contains the AAV rep and cap genes that were replaced in the AAV vector with the heterologous gene. *See* '237 patent at 3:3–7. The other necessary component is a vector containing accessory function genes. *See* '237 patent at 3:7–10. Accessory functions are "non-AAV derived viral and/or cellular functions upon which AAV is dependent for its replication," '237 patent at 7:41–43, and the vector containing those accessory function genes is an "accessory function vector." '237 patent at 8:1–3.

Once these three vectors have been introduced to the host cell, the heterologous gene is replicated and packaged into a recombinant virion. '237 patent at 3:11–13. The rAAV virions can then be used to treat a patient by infecting the patient's cells. '237 patent at 3:13–14. The heterologous gene enters and is expressed by the patient's cells but, because the patient's cells lack the AAV rep and cap genes and helper virus accessory function genes necessary for the rAAV to replicate and package its genome, the rAAV do not further replicate within the patient's cells. '237 patent at 3:15–19. The absence of AAV rep and cap genes in the patient's cells also means that the patient's cells will not produce unwanted wild-type or pseudo-wild-type AAV. '237 patent at 3:19–21.

Current methods of producing rAAV as of the '237 patent's filing, however, presented significant problems, including that the current methods produced too few rAAV

to be therapeutically useful and resulted in the production of replication-competent pseudo-wild-type AAV. *See* '237 patent at 3:22–29. Although many attempts had been made to address the formation of pseudo-wild-type AAV, none succeeded. *See* '237 patent at 3:36–37. Indeed, the stocks resulting from U.S. Patent No. 5,753, 500 (the "'500 patent"), filed on April 3, 1995 by Thomas E. Shenk et al., yielded between 0.01 and 10% wild-type AAV, a level of contamination that would be unacceptable for human trials. *See* '237 patent at 3:38–47.

The invention claimed by the '237 patent was intended to correct these deficiencies by "provid[ing] AAV helper functions for rAAV production that do not result in the formation of pseudo-wild-type AAV" and "that allow high efficiency production of rAAV." *See* '237 patent at 3:48–56. "The rAAV virions produced using the present invention may be used to introduce genetic material into animals, including humans, or isolated animal cells for a variety of research and therapeutic uses." '237 patent at 4:42–45. "For example, rAAV virions produced using the methods of the present invention may be used to express a protein in animals to gather preclinical data or to screen for potential drug candidates." '237 patent at 4:45–48. "Alternatively, the rAAV virions may be used to transfer genetic material into a human to cure a genetic defect or to effect a desired treatment." '237 patent at 4:48–51.

Dr. Peter Colosi filed Application No. 09/450,083 on November 29, 1999, which issued as the '237 patent on April 23, 2002. *See generally* Lambert Decl. Ex. A. The '237 patent was itself a continuation of Application No. 09/143,270, filed on August 28, 1998, and issued as U.S. Patent No. 6,001,650 (the "'650 patent"), itself a continuation of Application No. 09/107,708, filed on June 30, 1998, and issued as U.S. Patent No. 6,027,931 (the "'931 patent"), which was a continuation of Application No. 08/688,648, filed on July 29, 1996, and subsequently abandoned, which was a continuation of Application No. 08/510,790, filed on August 3, 1995, and issued as U.S. Patent No. 5,622,856. *See* '237 patent at 1:1–13.

/ / /

The ’237 patent, titled “High-Efficiency Wild-Type-Free AAV Helper Functions,” contains 17 claims, four of which are independent. *See generally id.* Each of the 17 claims begins with the phrase “[a] stock of recombinant adeno-associated virus.” *See generally id.* at 23:10–24:65.

B. The Assignment Agreement

In 2005, Defendant entered into a written Assignment Agreement with Avigen, Inc. (“Avigen”). First Am. Compl. (“FAC,” ECF No. 13) ¶ 6. Under this Agreement, Defendant “acquired from Avigen certain gene therapy intellectual property and gene therapy research and developmental programs. Avigen, in turn, received consideration up front and was eligible for specified milestone payments should certain events and/or conditions be met in the future.” *Id.* ¶ 7.

The technology acquired by Defendant included the ’237 patent. *Id.* ¶ 13. Defendant owes a milestone payment to Plaintiff under the Assignment Agreement “when the first patient is dosed or treated in a Phase I clinical study with a product that is covered by a claim of one of the Gene Therapy Patents issued in certain major markets” such as the United States. *Id.* ¶ 10.

In 2009, Avigen merged with Plaintiff and Plaintiff assumed all rights under the Assignment Agreement, including rights to milestone payments. *Id.* ¶ 11. In March 2014, Defendant informed Plaintiff that Defendant was “currently conducting a Phase 1 clinical trial of a gene therapy product for age-related macular degeneration named AAV-sFLT. [Defendant] explained that all patients in the clinical trial had already been dosed with AAV-sFLT.” *Id.* ¶ 12.

Plaintiff alleges that Defendant owes it the $1,000,000 milestone payment because AAV-sFLT is covered by the Agreement. *Id.* ¶ 16. As a result, Plaintiff alleges Defendant breached the Assignment Agreement by not paying Plaintiff. *Id.* ¶ 22. Defendant, on the other hand, contends that AAV-sFLT is not covered by the ’237 patent and, consequently, no milestone payment is owed. *See, e.g.*, Def.’s Br. at 2 n.1.

/ / /

II. Procedural History

On October 21, 2014, Plaintiff filed a Complaint against Defendant alleging two causes of action for breach of contract and breach of covenant of good faith and fair dealing. *See generally* ECF No. 1 ("Compl."). Although nominally a breach of contract action, Plaintiff conceded in its Complaint that its "right to relief depends on resolution of a substantial question of federal patent law." *Id.* ¶ 1.

Defendant moved to dismiss, *see generally* ECF No. 3, a request that the Honorable M. James Lorenz granted with leave to amend. *See generally* ECF No. 9. Plaintiff filed the operative amended complaint on September 4, 2015. *See generally* ECF No. 13. After Defendant filed its answer on September 28, 2015, *see generally* ECF No. 17, the Parties engaged in an Early Neutral Evaluation conference, *see* ECF No. 23, and proceeded to discovery. *See, e.g.*, ECF Nos. 25, 35.

On August 9, 2017, the case was reassigned to this Court. *See generally* ECF No. 55. On November 20, 2017, Defendant moved for summary judgment as to both of Plaintiff's causes of action. *See generally* ECF Nos. 70, 96. Because Defendant sought claim construction of the patent term "a stock of recombinant adeno-associated virus" as part of its motion for summary judgment, the Court set a status conference for April 19, 2018, to discuss the necessity of a claim construction hearing. *See generally* ECF No. 89. Following the hearing, the Court ordered the Parties to file a joint claim construction chart, *see* ECF No. 90, which they filed on May 3, 2018. *See generally* ECF No. 93.

In their initial joint claim construction chart, Plaintiff proposed that the disputed term "has a plain and ordinary meaning to one of ordinary skill in the art and no construction is necessary." *Id.* at 1. Defendant, on the other hand, proposed either that the disputed term (1) "exclude[] recombinant adeno-associated virus made using accessory functions derived from the herpes simplex type-1 (HSV-1) virus," or (2) mean "[a] stock of recombinant adeno-associated virus virions," to which the '237 patent's express definitions for a "recombinant AAV virion" and "accessory functions" would apply. *See id.* at 1–3.

/ / /

On June 6, 2018, the Court requested additional briefing from Plaintiff concerning Defendant's argument that "[p]rior art cited in the patent demonstrates that the invention is directed to rAAV virions," *see* ECF No. 97 (citing ECF No. 96 at 23), in response to which Plaintiff filed a supplemental brief. *See generally* ECF No. 100. On June 11, 2018, the Court invited the Parties to provide a tutorial or preliminary statement concerning the '237 patent and underlying technical issues. *See generally* ECF No. 98.

The Court held a hearing on Defendant's motion for summary judgment and the related claim construction issue on August 6, 2018. *See generally* ECF No. 111. At the end of the hearing, after months of briefing and hours of oral argument, *see generally* ECF Nos. 70, 86, 87, 93, 100, 113, Plaintiff's counsel contended that it had "not fully briefed claim construction" and requested "the opportunity to have additional briefing on this subject." ECF No. 113 ("Aug. 6, 2018 Tr.") at 91:14–25.

Consequently, the Court found that "it d[id] not have adequate information to engage in a sufficient claim construction analysis," denying without prejudice Defendant's motion for summary judgment, *see* ECF No. 112 at 1, and setting a second claim construction hearing. *See* ECF No. 115.

MOTION TO STRIKE

As a preliminary matter, Plaintiff requests that the Court strike Exhibits L, M, N, P, and Q to Defendant's Brief and those portions of Defendant's Brief relying on those exhibits, specifically page 13, line 9 through page 14, line 28,[2] for failure "to include [those

/ / /

/ / /

[2] Alternatively, Plaintiff requested that the Court grant it an additional five "pages to respond to Genzyme's improperly included evidence, and argument relating thereto, in MediciNova's Responsive Claim Construction Brief." Not. at 1. Plaintiff filed an *ex parte* motion to shorten the time for the Court to hear its Motion to Strike. *See generally* ECF No. 131. The Court denied Plaintiff's request and ordered it to file its responsive brief "in accordance with the provisions of Patent Local Rule 4.4(c) and Civil Local Rule 7.1(h)." ECF No. 133 at 1–2. Accordingly, Plaintiff's alternative request for additional pages was **DENIED**.

exhibits] in the parties' Joint Claim Construction Chart (ECF No. 117), as required by the Patent Local Rule 4.2([b])."[3] *See* ECF No. 130 ("Not.") at 1.

Plaintiff's Motion to Strike is brought pursuant to Federal Rule of Civil Procedure 37 and Patent Local Rule 4.2(b). Pursuant to Patent Local Rule 4.2(b),

> Each party's proposed construction of each disputed claim term, phrase, or clause, must identify all references from the specification or prosecution history that support that construction, and identify any extrinsic evidence known to the party on which it intends to rely either to support its proposed construction of the claim or to oppose any party's proposed construction of the claim, including, but not limited to, as permitted by law, dictionary definitions, citations to learned treatises and prior art, and testimony of percipient and expert witnesses.

Although Plaintiff does not specify whether its Motion to Strike is brought pursuant to Federal Rule of Civil Procedure 37(b) or (c), the Court concludes that Rule 37(b) is the proper provision. *See Pulse Eng'g, Inc. v. Mascon, Inc.*, No. 08CV0595JM(AJB), 2009 WL 250058, at *2 (S.D. Cal. Feb. 3, 2009) ("The relevant local patent rules here are 'essentially a series of case management orders.'") (citing *Integrated Circuit Sys. v. Realtek Semiconductor Co.*, 308 F. Supp. 2d 1106, 1107 (N.D. Cal. 2004)). Rule 37(b) gives courts the power to impose sanctions on parties who do not comply with their orders, including "prohibiting the disobedient party . . . from introducing designated matters in evidence." Fed. R. Civ. P. 37(b)(2)(A)(ii). Unless a proposed sanction implicates dismissal of an action, the court need not identify "willfulness, fault, or bad faith," even if the sanction is severe. *Yeti by Molly, Ltd. v. Deckers Outdoor Corp.*, 259 F.3d 1101, 1106 (9th Cir. 2001). A district court has wide discretion in determining the appropriateness of issuing sanctions. *Id.*; *Navellier v. Slettenm*, 262 F.3d 923, 947 (9th Cir. 2001). Exclusion of evidence is "particularly appropriate 'where the undisclosed information is significant and the party

[3] Although Plaintiff cites to Patent Local Rule 4.2(a), the language it cites comes from Patent Local Rule 4.2(b).

failing to make the timely disclosure lacked diligence.'" *Pulse Eng'g, Inc.*, 2009 WL 250058, at *2 (quoting *MGM Well Serv., Inc. v. Mega Lift Sys., LLC*, No. H-05-1634, 2007 WL 433283, at *2 (S.D. Tex. Jan. 24, 2007)).

Plaintiff claims that striking Defendant's Exhibits L, M, N, P, and Q and those portions of its Defendant's Brief relying on those exhibits is merited because Plaintiff "was prejudiced because it was not able to address [Defendant's new] exhibits and novel arguments in its Opening Claim Construction Brief (which is 25 pages, significantly longer than the 10 page Responsive Claim Construction Brief)." Mot. to Strike at 8. Defendant counters that the purportedly "new" exhibits "are all part of the prosecution history of the '237 patent, which Genzyme produced to MediciNova nearly two years ago," Opp'n at 5, and which Defendant listed in the Joint Claim Construction Chart. *See id.* at 6–10. Further, Defendant contends that it has not raised any "'new' arguments and legal theories" because its "position is straightforward and has been asserted . . . for two years." *Id.* at 5. Indeed, "MediciNova has had the benefit of possessing Genzyme's claim construction positions and evidence for a long time," which "starkly contrasts the position that Genzyme is in: MediciNova finally, after being reprimanded and forced by the Court, has engaged in claim construction, and thus Genzyme only recently received MediciNova's claim construction positions." *Id.* at 10–11.

The Court concludes that Plaintiff has not met its burden of showing that exclusion is warranted here. Not only did Plaintiff itself cite in its Brief to materials not listed in the Parties' Joint Claim Construction Chart, *see* Opp'n at 10 n.3; *see also* Declaration of M. Curt Lambert in Support of Opposition (ECF No. 138-1) ¶ 2, but Defendant did list prosecution history of the '237 patent in the Joint Claim Construction Chart. *See* ECF No. 117 at 8–9.[4] Further, the May 1, 2001 Amendment—listed by both Parties in the Joint Claim Construction Chart, *see id.* at 6 (Plaintiff), 8–9 (Defendant), was made in response to Defendant's Exhibits L, M, and N, *see* Opp'n at 7, and Plaintiff itself listed Exhibit P in

[4] Citations to ECF No. 117 refer to the CM/ECF pagination electronically stamped at the top of each page.

its Joint Claim Construction Chart. *See* ECF No. 117 at 6. In any event, Plaintiff has had the 239-page prosecution history of the '237 patent since February 6, 2017. Lambert Strike Decl. ¶ 3. Over two years later, nothing contained therein should be "new" to Plaintiff, particularly over four years into this litigation and on the second round of claim construction briefing.

Accordingly, the Court **DENIES** Plaintiff's Motion to Strike. *See, e.g.*, *Pulse Eng'g, Inc.*, 2009 WL 250058, at *3 ("[The defendant]'s disorderly revelation of supporting extrinsic evidence would seem to have little, if any, effect on [the plaintiff]'s ability to present its own interpretations of various patent terms. The court finds [the plaintiff] neither faces nor has faced any prejudice as a result of the reference disclosures.").

CLAIM CONSTRUCTION

I. Legal Standard

Claim construction is a matter of law for determination by the court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388 (1996) ("[J]udges, not juries, are the better suited to find the acquired meaning of patent terms.").

Words of a claim are "generally given their ordinary and customary meaning." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "[T]he 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." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). Because the inquiry into the meaning of claim terms is an objective one, "a court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004). "Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant

/ / /

/ / /

scientific principles, the meaning of technical terms, and the state of the art."[5] *Id.* (citing *Vitronics*, 90 F.3d at 1582–83).

Claim construction begins with an analysis of the words of the claims themselves. *See Scanner Techs. Corp. v. ICOS Vision Sys. Corp.*, 365 F.3d 1299, 1303 (Fed. Cir. 2004) (holding that claim construction "begins and ends" with a claim's actual words). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Phillips*, 415 F.3d at 1314. The meaning of a claim term as understood by ordinarily skilled artisans, however, often is not immediately apparent. *Id.* In those situations, the court looks to "sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." *Id.* Or, when a patentee "chooses to be his own lexicographer and use terms in a manner other than their ordinary meaning," the court can use the patentee's 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.

In examining the claims themselves, "the context in which a term is used can be highly instructive." *Phillips*, 415 F.3d at 1314. Moreover, "[o]ther claims of the patent in question, both asserted and unasserted can . . . be valuable sources of enlightenment as to the meaning of a claim term." *Id.* (citing *Vitronics*, 90 F.3d at 1582). "Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Conversely, under the doctrine of claim differentiation, "'different words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope.'" *Andersen*

/ / /

---

[5] The first three sources are considered "intrinsic evidence" of claim meaning, *see generally Phillips*, 415 F.3d at 1314–17, and are emphasized over "extrinsic evidence." *See id.* at 1317.

Corp. v. Fiber Composites, LLC, 474 F.3d 1361, 1369 (Fed. Cir. 2007) (quoting *Karlin Tech., Inc. v. Surgical Dynamics, Inc.*, 177 F.3d 968, 971–72 (Fed. Cir. 1999)).

"Importantly, the 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." *Phillips*, 415 F.3d at 1313. "The specification acts as a dictionary when it expressly defines terms used in the claims or when it defines them by implication." *Vitronics*, 90 F.3d at 1582. "In addition to providing contemporaneous technological context for defining claim terms, the patent applicant may also define a claim term in the specification 'in a manner inconsistent with its ordinary meaning.'" *Metabolite Labs., Inc. v. Lab. Corp. of Am.*, 370 F.3d 1354, 1360 (Fed. Cir. 2004). "Usually, [the specification] is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics*, 90 F.3d at 1582; *accord Phillips*, 415 F.3d at 1317 ("It is . . . entirely appropriate for a court, when conducting claim construction, to rely heavily on the written description for guidance as to the meaning of the claims.").

Patent claims should ordinarily be construed to encompass the preferred embodiments described in the specification, for "[a] claim construction that excludes a preferred embodiment . . . 'is rarely, if ever, correct.'" *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1285 (Fed. Cir. 2005) (quoting *Vitronics*, 90 F.3d at 1583). However, a court should not import limitations from the specification into the claims, *Phillips*, 415 F.3d at 1323 ("[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments."), absent a specific reference in the claims themselves, *Reinshaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998) ("[A] party wishing to use statements in the written description to confine or otherwise affect a patent's scope must, at the very least, point to a term or terms in the claim with which to draw in those statements.").

The patent's prosecution history, if in evidence, may also shed light on claim construction. *Vitronics*, 90 F.3d at 1582. "This history contains the complete record of all

proceedings before the Patent and Trademark Office [("PTO")], including any express representations made by the applicant regarding scope of the claims." *Id.* "Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Phillips*, 415 F.3d at 1317. Although the prosecution history "often lacks the clarity of the specification," it is nevertheless useful to show "how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

"In most situations, an analysis of the intrinsic evidence alone will resolve any ambiguity in a disputed claim term. In such circumstances, it is improper to rely on extrinsic evidence." *Vitronics*, 90 F.3d at 1583. Thus, expert testimony on the proper construction of disputed claim terms "may only be relied upon if the patent documents, taken as a whole, are insufficient to enable the court to construe disputed claim terms." *Id.* at 1585.

However, *Vitronics* does not state a rule of admissibility, nor does it "prohibit courts from examining extrinsic evidence, even where the patent document is itself clear." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999). As the Federal Circuit has made clear:

> [B]ecause extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence.

Phillips, 415 F.3d at 1319; *accord Key Pharms. v. Hercon Labs. Corp.*, 161 F.3d 709, 716 (Fed. Cir. 1998) ("[T]rial courts generally can hear expert testimony for background and education on the technology implicated by the presented claim construction issues, and trial courts have broad discretion in this regard."). The court is not "barred from considering any particular sources or required to analyze sources in any specific sequence, as long as those sources are not used to contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Phillips*, 415 F.3d at 1324; *see also Biagro W. Sales, Inc.*

v. Grow More, Inc., 423 F.3d 1296, 1302 (Fed. Cir. 2005) ("Extrinsic evidence, such as expert testimony, may be useful in claim construction, but it should be considered in the context of the intrinsic evidence.").

II. Analysis

In their Joint Claim Construction Chart, the Parties identify the sole disputed claim term as "a stock of recombinant adeno-associated virus," also abbreviated as "a stock of recombinant AAV" or "a stock of rAAV." ECF No. 117 at 2, 6. Each of the 17 claims of the '237 patent claims begins with—and therefore claims—"[a] stock of recombinant adeno-associated virus." *See* '237 patent at 23:10–24:64.

Although there are four independent claims, *see* '237 patent at 23:11–26 (claim 1), 23:37–42 (claim 4), 23:59–24:19 (claim 8), 24:32–37 (claim 11), the Parties' Opening Briefs focus on claim 1, which they agree is representative. *See*, *e.g.*, Def.'s Br. at 2–3; Pl.'s Br. at 10–11. Claim 1 of the '237 patent claims:

> A stock of recombinant adeno-associated virus free of wild-type adeno-associated virus, wherein the recombinant adeno-associated virus comprises a packaged recombinant adeno-associated virus vector containing a heterologous gene of interest but lacking adeno-associated virus genes required for replication or packaging of said adeno-associated virus vector, and wherein wild-type adeno-associated virus is not detectable by a method comprising:
>
> (a) isolating viral DNA from the stock of recombinant adeno-associated virus;
>
> (b) performing about 35 rounds of polymerase chain reaction ("PCR") on the viral DNA under PCR conditions designed to selectively amplify DNA sequences from wild-type adeno-associated virus; and
>
> (c) assaying for the presence or absence of amplified wild-type adeno-associated virus DNA sequences.

'237 patent 23:10–26.

/ / /

A. Plaintiff's Proposed Construction

Plaintiff proposes that the Court construe the term "[a] stock of recombinant adeno-associated virus" to mean "[a] supply of genetically altered adeno-associated virus." ECF No. 117 at 6 (emphasis omitted); *see also* Pl.'s Br. at 1.

At the first hearing, the Court cautioned Plaintiff that its "proposal of 'plain and ordinary meaning [wa]s unhelpful and it would be erroneous to construe such a technical term as its plain and ordinary meaning." Aug. 6, 2018 Tr. at 4:13–16. The Court also noted that Plaintiff had failed to define the relevant, disputed terms. *See id.* at 92:13–17, 94:9–16; *see also id.* at 98:16–99:7. Now, however, on its second bite at the claim construction apple, Plaintiff urges the Court to construe the term "stock" to mean "supply" based on extrinsic evidence, *see* Pl.'s Br. at 14–16, and to construe "recombinant" to mean "genetically altered," as expressly defined by the '237 patent. *See id.* 13–14 (citing '237 patent at 8:12–15). Plaintiff maintains that "[t]he [c]laim [t]erm '[a]deno-[a]ssociated [v]irus' [d]oes [n]ot [r]equire [c]onstruction." *Id.* at 16 (emphasis omitted), because "claim 1 expressly specifies that the 'stock' of claim 1 is composed of virus in the form of AAV vector." *Id.* at 16–17 (emphasis in original). In other words, as Plaintiff's counsel explained at the June 18, 2019 hearing, the Court need only to continue reading claim 1 to construe properly the disputed term. *See* ECF No. 147 ("June 18, 2019 Tr.") at 79:26–23.

The Court must agree with Defendant that "'[s]upply' and 'genetically altered' are unhelpful synonyms for the undisputed terms 'stock' and 'recombinant.'" *See* Def.'s Resp. at 1 (emphasis omitted). And the Court would not have held a claim construction hearing—much less a second claim construction hearing—if the disputed term had a plain and ordinary meaning. It is unconscionable that, after over a year of countless hours spent briefing and arguing claim construction, *see, e.g.*, ECF Nos. 70, 90, 93, 97–98, 100, 103, 111–15, 117, 123, 126, 134, 135, 140, 144, 147, the only real construction Plaintiff offers amounts to "not Defendant's."

Further, Plaintiff errs in at least three respects to the extent that it contends that "a stock of recombinant adeno-associated virus" is simply "a supply of genetically-altered

adeno-associated virus vector." *See* Pl.'s Br. at 10–10; *see also*, *e.g.*, June 18, 2019 Tr. at 79:16–23. First, while independent claims 1 and 8 provide that the stock "comprises a . . . recombinant adeno-associated virus vector," *see* '237 patent at 23:12–14 (claim 1), 23:61–62 (claim 8), independent claims 4 and 11 do not. *See generally* '237 patent at 23:37–42 (claim 4), 24:32–37 (claim 11).

Second, Plaintiff's proposal is an oversimplification because the stock claimed in claim 1 is explicitly composed of "a *packaged* recombinant adeno-associated virus vector containing a heterologous gene of interest but lacking adeno-associated virus genes required for replication or packaging of said adeno associated virus vector, and *wherein wild-type adeno-associated virus is not detectable*" following 35 rounds of PCR. '237 patent at 23:13–18 (emphasis added). Nonetheless, Plaintiff contends that "it is not necessary that the Court construe [the term 'packaged']," Pl.'s Br. at 12 n.2, and that the "additional, other requirements [in claim 1, including that the stock contain undetectable levels of wild-type AAV,] . . . are not in dispute or are not central to an understanding of the present claim construction dispute between the parties." *Id.* at 13. For the reasons discussed below, *see infra* Section II.B, the Court disagrees.

Third, Plaintiff's proposal is entirely divorced from the specification (and other intrinsic evidence), which outlines in great detail a process through which a host cell is transfected with three separate vectors to produce rAAV virions. *See generally* '237 patent Abstract; '237 patent at Fig. 5; '237 patent 1:19–18:47; *see also supra* Section II.B..

Because Plaintiff has, once again, offered a non-construction of the relevant, disputed terms, the Court **DECLINES** to adopt Plaintiff's proposed construction.

B. Defendant's Proposed Construction(s)

Defendant offers two proposed constructions. ECF No. 117 at 6–8. Defendant first proposes that "[t]he term 'a stock of recombinant adeno-associated virus' excludes recombinant adeno-associated virus made using accessory functions derived from the herpes simplex type-1 (HSV-1) virus." *Id.* at 6 (emphasis omitted). Alternatively, Defendant proposes that "'[a] stock of recombinant adeno-associated virus' means 'A stock

of recombinant adeno-associated virus virions,'" meaning that the express definitions for a "recombinant AAV virion" and "accessory functions" in the '237 patent would apply. *Id.* at 6–8 (emphasis omitted). In essence, both of Defendant's proposed constructions ask the Court to construe the term "a stock of recombinant adeno-associated virus" to be "a stock of 'rAAV virions,' which [i]s expressly defined [in the '237 patent] to include a limitation that they cannot be produced using accessory functions derived from HSV-1." Def.'s Br. at 7–8.

1. Defendant's Arguments in Favor of Its Proposed Construction(s)

Defendant points to a wealth of intrinsic evidence it claims supports its proposed construction(s) that the claimed stock is composed of rAAV virions, including language from the '237 patent's claims and specification, the prosecution history of the '237 patent, and the prior art cited in the '237 patent. Def.'s Br. at 8–17. Defendant also relies on extrinsic evidence, including the declarations and testimony of its expert witness, Dr. Barry J. Byrne, and Plaintiff's expert witness, Dr. Scott R. Burger. *See id.* at 17–19.

a. The Claims of the '237 Patent

As always, the Court begins with the language of the claim itself. *Scanner Techs. Corp.*, 365 F.3d at 1303 (holding that claim construction "begins and ends" with a claim's actual words). Although neither the disputed term nor the claim as a whole includes the word "virions," Defendant nonetheless contends that claim 1 is necessarily directed to rAAV virions because of the requirements that (1) the rAAV vector be "packaged" and, (2) the resultant stock have an undetectable level of wild-type AAV following 35 rounds of PCR.

i. <u>"Packaged"</u>

Defendant first contends that the use of the word "packaged" in claim 1 indicates that the claim is directed to rAAV virions. *See* Def.'s Br. at 11–12; *see also* '237 patent at 23:12–14 (claiming a stock of rAAV "wherein the recombinant adeno-associated virus comprises a *packaged* recombinant adeno-associated virus vector") (emphasis added). According to Defendant, "[t]he '237 specification could not be more clear that when an

rAAV vector is packaged, it forms an rAAV virion." Def.'s Br. at 11. For example, Defendant notes, the specification provides that "[s]ubsequent infection by a helper virus 'rescues' the integrated genome, allowing it to replicate and ***package*** its genome into infectious ***AAV virions***." *Id.* (quoting '237 patent at 2:51–54) (emphasis in original). Similarly, the specification provides that, "[o]nce these factors come together, the heterologous gene is replicated and ***packaged*** as though it were a wild-type AAV genome, ***forming a recombinant virion***," *id.* (quoting '237 patent at 3:11–13) (emphasis in original), and, "[i]n this regard, single-stranded AAV nucleic acid molecules of either complementary sense, i.e., 'sense' or 'antisense' strands, can be ***packaged*** into any one ***AAV virion*** and both strands are equally infectious." *Id.* (quoting '237 patent at 8:15–22) (emphasis in original). Defendant also notes that "the express definitions show that when a vector is 'packaged,' it is a virion," relying on the definition of "recombinant AAV virion," which notes that "the host cell is rendered capable of encoding AAV polypeptides that are required for ***packaging*** the AAV vector . . . into infectious ***recombinant virion particles***." *Id.* at 11–12 (quoting '237 patent at 8:22–32) (emphasis in original). In sum, Defendant is asking the Court to look to the specification, which refers to virions as "packaged," to read the word "packaged" in claim 1 to means that stock of rAAV must refer to rAAV virions.

Plaintiff counters that "there is nothing in the Specification that limits 'packaging' to virions." Pl.'s Resp. at 3. To the contrary, Plaintiff claims, "the Figures in the '237 Patent . . . illustrate an AAV vector that is packaged into a plasmid." *Id.*

While a court interprets claim terms in light of the specification, it should generally not "import[] limitations from the specification into the claims absent a clear disclaimer of claim scope." *Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1373 (Fed. Cir. 2007). "[T]he distinction between using the specification to interpret the meaning of a claim and importing limitations from the specification into the claim can be a difficult one to apply in practice." *Phillips*, 415 F.3d at 1323. In walking this "tightrope," *Andersen*, 474 F.3d at 1373, the court hews to the question of "how a person of ordinary skill in the

art would understand the claim terms," *Phillips*, 415 F.3d at 1323. "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Phillips*, 415 F.3d at 1316 (internal quotation marks omitted).

The specification defines a "vector" as "any genetic element, such as a plasmid, phage, transposon, cosmid, chromosome, artificial chromosome, virus, virion, etc., which is capable of replication when associated with the proper control elements and which can transfer gene sequences between cells." '237 patent at 5:46–50. "Thus, the term includes cloning and expression vehicles, as well as viral vectors." '237 patent at 5:50–52. The express definition of the term "vector" therefore indicates it can take many forms.

Further review of the specification confirms that the '237 patent comprises more than one type of "vector." For example, there are "AAV helper constructs," *see* '237 patent at 7:22–40, and "accessory function vectors," *see* '237 patent at 8:1–11, both of which may be "in the form of a plasmid, phage, transposon, cosmid or virus." *Compare* '237 patent at 7:31–33, *with* '237 patent at 8:9–10. The '237 patent also contemplates "AAV vectors," *see* '237 patent at 6:64–7:10, which are "vector[s] derived from an adeno-associated virus serotype," '237 patent at 6:64–65, that "include at least those sequences required in cis for replication and packaging (e.g., functional ITRs) of the virus." '237 patent at 7:5–7. The interplay of these various vectors can be seen in the '237 patent's definition of a rAAV virion, '237 patent at 8:22–32, which "is produced in a suitable host cell comprising an AAV vector, AAV helper functions, and accessory functions," '237 patent at 8:26–28, by which "the host cell is rendered capable of encoding AAV polypeptides that are required for packaging the AAV vector (containing a recombinant nucleotide sequence of interest) into infectious recombinant virion particles for subsequent gene delivery." '237 patent at 8:28–32.

This is to say that Plaintiff is not incorrect in saying that the specification of the '237 patent speaks of certain vectors taking non-virion forms; however, the relevant question is whether the specific vector claimed in claim 1—"a packaged recombinant adeno-

associated virus vector containing a heterologous gene of interest but lacking adeno-associated virus genes required for replication or packaging of said adeno-associated virus vector," '237 patent at 23:13–17—must be packaged as a virion, per Defendant, or whether it may be take the form of a virion or other vector, as Plaintiff would have it.

Defendant's citations to the specification, discussed above, are persuasive support in favor of its construction(s). *See, e.g.*, '237 patent at 2:51–54 ("Subsequent infection by a helper virus 'rescues' the integrated genome, allowing it to replicate and *package* its genome into infectious AAV virions.") (emphasis added); '237 patent at 3:11–13 ("Once these factors come together, the heterologous gene is replicated and *packaged* as though it were a wild-type AAV genome, forming a recombinant virion.") (emphasis added); '237 patent at 8:15–22 ("In this regard, single-stranded AAV nucleic acid molecules of either complementary sense, i.e., 'sense' or 'antisense' strands, can be *packaged* into any one AAV virion and both strands are equally infectious.") (emphasis added). A careful review of all uses of the term "packag[ing]" in the specification demonstrates that the term is always used to refer to the packaging of the viral genome into a virion. *See generally* '237 patent.

Plaintiff cites no evidence within the '237 patent compelling a different result. Instead, Plaintiff cites to "[e]xamples of different types of vectors given in the '237 Patent." *See* Pl.'s Br. at 12 (citing '237 patent at 5:46–48). Plaintiff's citation, however, is to the general definition of "vector," a definition that encompasses the various types of vectors discussed within the '237 patent rather than the specific vector claimed by claim 1. Plaintiff also points to an illustration of "an AAV vector inserted into a second vector" from Figure 1 of the '237 patent. *See id.* at 12–13 (citing '237 patent at Fig. 1). But this "AAV Vector"—however packaged—is clearly depicted as a precursor to the resultant claimed stock and not the claimed stock itself. *See* '237 patent at Fig. 1.

The testimony of the Parties' experts serves only to bolster Defendant's proposed construction(s). For example, Defendant's expert, Dr. Byrne, opines that "the use of the word 'packaged' would indicate to a person of ordinary skill in the art that the genetic

material that is being described is a virion, i.e., a complete virus particle." Lambert Decl. Ex. K at 496 ¶ 8; *see also* Lambert Decl. Ex. K at 517–18 ("The use of the word 'packaged' indicates to a person of ordinary skill in the art that the genetic material that is being described is a virion, in other words a complete virus particle. 'Packaged' would not be used to describe a *component* of a virion, such as a viral genome or vector."). Even Plaintiff's expert, Dr. Scott R. Burger, agreed at his November 15, 2017 deposition, testifying that the term "packaged" meant "[t]he final assembly step of the intact virus particle," Lambert Decl. Ex. B at 55:14–17, *i.e.*, a virion.[6] *See id.* at 67:22–68:20. Consequently, the requirement in claim 1 that the rAAV vector be "packaged" supports Defendant's proposed construction(s).[7]

---

[6] Defendant intimates in its responsive brief that Dr. Burger's position changed materially between his first deposition on November 15, 2017, and when Plaintiff first formulated its claim construction a year later. *See* Def.'s Resp. at 5. Indeed, in his November 16, 2018 expert report, Dr. Burger opined that a person of ordinary skill in the art "would have understood the requirements that the rAAV vector be 'packaged' in one of two ways." Declaration of Dr. Scott R. Burger re: Claim Constr. ("Burger Decl.," ECF No. 126-1) ¶ 62. "First, the requirements that the rAAV vector be 'packaged' could be understood to simply refer to the fact that the genetic material in the AAV vector is 'packaged' between the two ITRs." *Id.* ¶ 63. This proposed construction, however, makes little sense in the context of the '237 patent, which defines an AAV vector "to include at least those sequences required in cis for replication and packaging (e.g., functional ITRs) of the virus." '237 patent at 7:4–7. Because the AAV vector necessarily includes ITRs per the express definitions of the '237 patent, it seems unlikely that a person of ordinary skill in the art reading the '237 patent would have understood the term "packaged" in claim one to mean that the AAV vector is packaged between two ITRs. *See* Def.'s Resp. at 5; *see also* Second Declaration of M. Curt Lambert in Support of Def.'s Br. ("Second Lambert Decl.") Ex. U at 51:13–30 (Dr. Burger testifying in December 2018: "Q. Must an AAV vector have ITRs? A. Yes."). Further, the definition for AAV vector itself contemplates a different sort of "packaging," which would seem inconsistent with Dr. Burger's first proposal: "The ITRs need not be the wild-type nucleotide sequences, and may be altered, e.g., by the insertion, deletion or substitution of nucleotides, so long as the sequences provide for functional rescue, replication and *packaging*." '237 patent at 7:7–10 (emphasis added).

Alternatively, Dr. Burger opines that "the requirement that the rAAV vector be 'packaged' could also be understood to require that the AAV vector is inserted into a vector of any of the types listed in the specification, including 'a plasmid, phage, transposon, cosmid, chromosome, artificial chromosome, virus, virion, etc[.]'" Burger Decl. ¶ 64 (alteration in original) (quoting '237 patent at 5:46–52). Again, this citation to the general definition in the '237 patent for the term "vector" is not inconsistent with Defendant's proposed construction(s). *See supra* Section II.B.1.a.i.

[7] Plaintiff's argument that the term "packaged" is absent from independent claims 4 and 11, *see* Pl.'s Resp. at 3, is a valid point but does not compel a different result given the additional intrinsic and extrinsic evidence supporting Defendant's construction(s) discussed below.

ii. Undetectable Level of Wild-Type AAV

Claim 1's requirement the stock have an undetectable level of wild-type or pseudo-wild-type AAV, an argument Defendant raised only in response to Plaintiff's Brief, *see* Def.'s Resp. at 6–7, also bolsters Defendant's proposed construction(s).

Specifically, claim 1 claims "[a] stock of recombinant adeno-associated virus *free of wild-type adeno-associated virus*, . . . and wherein *wild-type adeno associated virus is not detectable* by" 35 rounds of PCR. *See* '237 patent at 23:11–25 (emphasis added). As Defendant notes, *see* Def.'s Resp. at 6, the '237 patent uses the term wild-type AAV to refer to pseudo-wild-type AAV, which are explicitly defined as "replication-competent AAV virions." '237 patent at 11:43–50. This would mean that the stock claimed by the '237 patent contains undetectable levels of these undesirable AAV virions. Dr. Burger conceded, however, that "a stock of rAAV plasmids [cannot] contain wild-type AAV virions" or "pseudo-wild-type AAV virions."[8] *See* Second Lambert Decl. Ex. U at 41:13–23. Consequently, claim 1's requirement that the resultant stock have an undetectable level of wild-type adeno-associated virus following 35 rounds of PCR would be superfluous if the claim were construed such that the resultant stock were composed of anything other than virions. *See* Def.'s Resp. at 7.

As the Federal Circuit has often cautioned, "[a] claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so." *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005). Consequently, the

[8] At the June 18, 2019 hearing, Plaintiff accused Defendant of misrepresenting Dr. Burger's testimony on this point, noting that Dr. Burger later testified that he was "confused" by the question and that a stock of rAAV plasmids could indeed be contaminated with wild-type or pseudo-wild-type rAAV virions. June 18, 2019 Tr. at 76:13–77:18; *see also* Dec. 18, 2018 Burger Dep. at 70:9–22 (ECF No. 146). As Defendant explained, however, Dr. Burger only "corrected" his testimony after discussing his answer with counsel during a break. June 18, 2019 Tr. at 88:15–90:22; *see also* Dec. 18, 2018 Burger Dep. at 72:12–73:6 (ECF No. 145). The Court therefore affords greater weight to Dr. Burger's prior testimony, which has the additional benefit of being corroborated by Dr. Byrne. *See, e.g.*, June 18, 2019 Tr. at 96:23–14 (explaining that, as of priority date of the '237 patent, wild-type and pseudo-wild-type contamination of rAAV plasmids was a non-issue and that the novelty of the '237 patent was in its ability to produce contaminant-free stocks of rAAV virions).

claim language concerning an undetectable level of wild-type AAV also bolsters Defendant's proposed construction(s). This is particularly true given that each of the seventeen claims of the '237 patent emphasizes the undetectability of wild-type (or pseudo-wild-type) AAV following 35 rounds of PCR amplification. *See* '237 patent at 23:10–24:65.

b. The Specification of the '237 Patent

The Court next turns to the specification of the '237 patent, as "[c]laims must be read in view of the specification, of which they are a part." *Vitronics Corp.*, 90 F.3d at 1582 (quoting *Markman*, 52 F.3d at 979). Defendant contends that the specification of the '237 patent supports its construction(s) because the specification (1) often describes the "present invention" as being directed to rAAV virions, Def.'s Br. at 8–10; (2) uses the terms "AAV" and "AAV virions" interchangeably, *id.* at 10–11; and (3) makes clear that the stocks are intended for clinical applications, Def.'s Resp. at 7–8.

i. "The Present Invention"

Defendant first contends that the specification of the '237 patent often describes the "present invention" as being directed to rAAV virions. *See* Def.'s Br. at 9–10. For example, "[t]he Abstract section states that "[t]he ***present invention*** provides methods and compositions for producing high titer, wild-type-free preparations of ***recombinant AAV ("rAAV") virions***." *Id.* at 9 (quoting '237 patent Abstract) (emphasis in original). "Similarly, in the 'Field of the Invention' section, the '237 patent states: 'The ***present invention*** related to adeno-associated virus (AAV) helper function systems for use in ***recombinant AAV (rAAV) virion*** production." *Id.* (quoting '237 patent at 1:21–26).

> The Brief Summary of the Invention section of the '237 patent likewise discloses that ***rAAV virions*** are produced using the ***present invention***:
>
> > The rAAV virions produced using the present invention may be used to introduce genetic material into animals, including humans, or isolated animal cells for a variety of research and therapeutic uses. For example, rAAV virions

> produced using the methods of the present invention may be used to express a protein in animals to gather preclinical data or to screen for potential drug candidates. Alternatively, the rAAV virions may be used to transfer genetic material into a human to cure a genetic defect or to effect a desired treatment.

Id. at 9–10 (quoting ’237 patent at 4:42–51).

> The General Methods section of the ’237 patent further makes clear that ***rAAV virion*** production is ***the invention***:
>
> > It is a primary object of ***the present invention*** to provide improved AAV helper function vectors and host cells useful in the high-efficiency production of ***rAAV virions*** that can subsequently be used in gene transfer methods.
> >
> > * * * * *
> >
> > In one embodiment, a nucleic acid molecule encoding one or more AAV helper functions for supporting ***rAAV virion*** production in an animal host cell is provided.
> >
> > * * * * *
> >
> > The AAV helper function vectors of ***the present invention*** can be used in a variety of systems for ***rAAV virion*** production.

Id. at 10 (quoting ’237 patent at 11:53–60, 12:9–11, 13:62–64) (emphasis in original).

Plaintiff counters that “the words present invention [] occur *33 times* within the ’237 Patent itself. Sometimes they refer to virions. We have examples of where they are referring to stock. . . There are other times where the present invention is described as being directed towards vectors.” Pl.’s Resp. at 3 (quoting Aug. 6, 2018 Tr. at 65:16–24) (emphasis in original). “Thus, the idea that the words ‘the present invention’ could be used to limit the claims of the patents to virions is unavailing.” *Id.* (citing ’237 patent at 5:27–30 (“. . . the AAV helper function vectors of the present invention . . .”); ’237 patent at 3:67–4:2 (“The nucleic acids of the present invention . . .”)).

In *Honeywell International, Inc. v. ITT Industries, Inc.*, 452 F.3d 1312 (Fed. Cir. 2006), the Federal Circuit found that the use of “present invention language” within the

specification may be significant in deciding whether claim terms can be limited by certain disclosed embodiments. *Id.* at 1318. In *Honeywell*, a fuel filter was discussed in the specification not merely as a preferred embodiment, but also as a limitation to the patent scope because on at least four occasions the specification referred to the fuel filter as "this invention" or "the present invention." *Id.* The Federal Circuit therefore concluded that "[t]he public is entitled to take the patentee at his word and the word was that the invention is a fuel filter." *Id.*

Similarly, in *Verizon Services Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295 (Fed. Cir. 2007), the Federal Circuit reiterated that "when a patent [thus] describes the features of the 'present invention' as a whole, this description limits the scope of the invention." *Id.* at 1308. But "use of the phrase 'present invention' or 'this invention' is not always so limiting, such as where the references to a certain limitation as being the 'invention' are not uniform, or where other portions of the intrinsic evidence do not support applying the limitation to the entire patent." *Absolute Software, Inc. v. Stealth Signal, Inc.*, 659 F.3d 1121, 1136 (Fed. Cir. 2011).

Here, Plaintiff is correct that the specification of the '237 patent does not uniformly limit the use of the phrase "the present invention" to rAAV virions; nonetheless, it is clear from the language of the specification that the intended *end product* of the claimed invention is composed of virions. In the Abstract, for example, the Inventor uses "the present invention" to refer to "novel nucleic acids encoding AAV helper functions and AAV helper function vectors," as well as to "host cells transfected by the claimed nucleic acids[and] methods of using the claimed vectors." *See* '237 patent Abstract. But the Inventor also provides that "[t]he present invention provides methods and compositions for producing high titer, wild-type-free preparations of recombinant adeno-associated virus ("rAAV") virions. . . . The present invention also includes . . . rAAV virions produced by such methods." '237 patent Abstract. As discussed above, *see supra* Section II.B.a.i, the specification makes clear that the '237 patent comprises various vectors that ultimately

/ / /

produce rAAV virions. Consequently, the '237 patent uses the term "the present invention" to refer to the antecedent vectors and the resultant stock.

This is evident throughout the specification. The Field of the Invention section, for example, relates to AAV helper function systems and the resultant rAAV virions: "The present invention relates to adeno-associated virus (AAV) helper function systems for use in recombinant AAV (rAAV) virion production." '237 patent at 1:19–21 (emphasis added). Similarly, the Brief Summary of the Invention explains that the claimed invention includes accessory function vectors and the rAAV virions produced through their use: "The present invention further provides methods of using accessory function vectors to produce rAAV and the rAAV virions produced by such methods." '237 patent at 4:24–26; *see also* '237 patent at 4:42–51 ("The rAAV virions produced using the present invention may be used to introduce genetic material into animals, including humans, or isolated animal cells for a variety of research and therapeutic uses. For example, rAAV virions produced using the methods of the present invention may be used to express a protein in animals to gather preclinical data or to screen for potential drug candidates. Alternatively, the rAAV virions may be used to transfer genetic material into a human to cure a genetic defect or to effect a desired treatment."). The Detailed Description of the Invention also makes clear that the invention is directed to rAAV virions and their precursors:

> It is a primary object of the present invention to provide improved AAV helper function vectors and host cells useful in the high-efficiency production of rAAV virions that can subsequently be used in gene transfer methods. More particularly, it is an object of the present invention to provide AAV helper function vectors and host cells that support production of commercially useful amounts of pseudo-wild-type-free rAAV virions.

'237 patent at 11:53–60. Consequently, the specification supports Defendant's contention that the end product—or "stock"—of the claimed invention is composed of rAAV virions.

/ / /

/ / /

ii. Interchangeable Usage

Defendant also argues that "the patent specification contains other language that shows that the claimed rAAV was intended to be rAAV virions." Def.'s Br. at 10. For example, "[t]he specification states that 'conventional AAV rep/cap vectors produce pseudo-wild-type **AAV virions**, as shown in FIGS. 1–3. By contrast, the AAV helper constructs of the present invention do not produce detectable pseudo-wild-type **AAV**, as shown in FIG. 4." *Id.* (quoting '237 patent at 18:34–38) (emphasis in original). According to Defendant, "[t]he terms 'pseudo-wild-type AAV virions' and 'pseudo-wild-type AAV' are used synonymously, demonstrating that the individual AAV virions make up AAV." *Id.* Similarly, "[t]he Definitions section of the patent further uses the terms 'virus' and 'virion' in a way that indicates that 'virion' is the individual virus particle of rAAV, and thus rAAV is composed of rAAV virions." *Id.* For example, "'wild-type AAV' is defined in the patent to include 'both wild-type and pseudo-wild-type AAV,' where pseudo-wild-type AAV 'are replication-competent AAV ***virions*** . . . .'" *Id.* (quoting '237 patent at 11:43–45) (emphasis in original).

Plaintiff responds that "a stock of 'virus' and a stock of 'virions' are not synonymous." Pl.'s Resp. at 6 (quoting Pl.'s Br. at 21–22). That may be true generally, but the question here is whether the Inventor has used the terms "AAV" and "AAV virions" synonymously *within the '237 patent*. Defendant has introduced evidence that the Inventor does not consistently distinguish between the terms AAV and AAV virions, further supporting Defendant's proposed construction(s).

The Court notes that the Figures in the '237 patent also support Defendant's argument. Figure 4 "depicts the viral products generated by" the '237 patent, through which "[p]seudo-wild-type AAV are not detected." '237 patent at 5:1–3. The end-product is depicted and labelled as an "AAV Vector." *See* '237 patent at Fig. 4. Figure 5, however, "illustrates the three-plasmic method of generating recombinant AAV," Nov. 15, 2017

/ / /

/ / /

Burger Tr. at 49:21–24 (ECF No. 145),[9] the method described throughout the '237 patent. *See generally, e.g.*, '237 patent at 2:15–4:51, 11:53–14:38. As Dr. Burger conceded at his November 15, 2017 deposition, Figure 5 depicts virions as the result of the co-transfection process described by the '237 patent. *See* Nov. 15, 2017 Burger Tr. at 49:25–50:25 (ECF No. 145). This, too, would support Defendant's contention that the claimed stock of recombinant vector is a stock of rAAV virions.

iii. Use in Clinical Trials

Defendant also notes in its responsive brief that "stocks of virions, not stocks of plasmids, are contemplated by the invention because the stocks of the invention are expressly described as contemplated for use in virion-based clinical trials." Def.'s Resp. at 7–8. For example, "[t]he '237 patent expressly criticizes the prior art stocks for having high contamination that makes them 'unacceptable for human clinical trials,'" *id.* at 8 (quoting '237 patent at 3:45–48), while "expressly describ[ing] using 'rAAV virions produced using the present invention' in clinical trials." *Id.* (citing '237 patent at 3:13–16 ("When a patient's cells are infected with the resulting rAAV virions . . . ."); '237 patent at 4:42–45 ("The rAAV virions produced using the present invention may be used to introduce genetic material into animals, including humans . . . .")). On the other hand, "stocks of *plasmids* are not used therapeutically in virion-based clinical trials." *Id.* Defendant therefore urges that "MediciNova's proposed claim construction—crafted to capture stocks of plasmids—is inconsistent with the express intent of the '237 patent, [and therefore] it cannot be the correct construction." *Id.*

/ / /

/ / /

/ / /

[9] Defendant provided the Court with pages 49 through 50 of Dr. Burger's November 15, 2017 deposition transcript, which were not included in either Exhibit B to the Lambert Declaration or Exhibit T to the Second Lambert Declaration, during the June 18, 2019 hearing, *see* June 18, 2019 Tr. at 57:11–18, subsequently filed as ECF No. 145.

At the June 18, 2019 hearing, Plaintiff claimed that stocks of rAAV plasmids can also be used in clinical trials. June 18, 2019 Tr. at 13:6–9, 16:17–21, 77:25–78:7. This may be true,[10] but the specification refers specifically to research and therapeutic uses for the resultant virions:

> The rAAV virions produced using the present invention may be used to introduce genetic material into animals, including humans, or isolated animal cells for a variety of research and therapeutic uses. For example, rAAV virions produced using the methods of the present invention may be used to express a protein in animals to gather preclinical data or to screen for potential drug candidates. Alternatively, the rAAV virions may be used to transfer genetic material into a human to cure a genetic defect or to effect a desired treatment.

'237 patent at 4:42–51. The specification's explicit reference to using the '237 patent's resultant rAAV virions for clinical applications therefore further bolsters Defendant's proposed construction(s).[11]

c. The Prosecution History of the '237 Patent

Where, as here, *see, e.g.*, Lambert Decl. Exs. C–D, L, P–Q, the prosecution history of the patent is in evidence, the Court may consider it in determining the meaning of the claims. *See Vitronics Corp.*, 90 F.3d at 1582–83. Defendant argues that "[t]he prosecution

---

[10] Not surprisingly, Dr. Byrne and Dr. Burger offer conflicting views on this topic. *Compare* June 18, 2019 Tr. at 21:4–22:14 (Dr. Byrne testifying that virions are used for clinical applications), *with id.* at 13:6–9, 16:17–21 (Dr. Burger testifying that plasmids may be used for clinical applications).

[11] In further support of its argument, Defendant notes that the Applicant also expressed the suitability of the resultant rAAV virions for clinical applications during the prosecution of the '237 patent. *See* Def.'s Resp. at 8 (citing Lambert Decl. Ex. C at 62 ("[T]he stocks of the present invention are wild-type free when produced at large scale and when tested using sensitive PCR-based assays. Furthermore, despite the fact that these stocks have several orders of magnitude more recombinant virions than the prior stocks, the present stocks still have no detectable wt-AAV. Thus, these stocks are better suited for clinical applications than any of the prior stocks."); Second Lambert Decl. Ex. V at 62 ¶ 4 ("I believe the development of recombinant AAV stocks that are free of contaminating wild-type AAV, i.e., recombinant AAV stocks suitable for human gene therapy trials, and the ability to raise money for such clinical trials will be significantly impaired if the examination of the above-identified patent application is delayed.")).

history . . . conclusively demonstrates that the claimed invention is directed to rAAV virions." Def.'s Br. at 12.

First, Defendant points to an Amendment and Response to Office Action dated May 1, 2001, in which the Applicant stated:

> [T]he ***stocks of the present invention*** have been shown to substantially eliminate both homologous and nonhomologous recombination. Therefore, the ***stocks of the present invention*** are wild-type free when produced at large scale and when tested using sensitive PCR-based assays. Furthermore, despite the fact that ***these stocks have several orders of magnitude more recombinant virions*** than the prior stocks, the ***present stocks*** still have no detectable wt-AAV. Thus, ***these stocks*** are better suited for clinical application than any of the prior stocks.

Id. (quoting Lambert Decl. Ex. C at 62) (emphasis in original). Consequently, Defendant contends, "the Applicant clearly and unequivocally . . . confirmed that '***these stocks*** have . . . ***recombinant virions***." *Id.* (emphasis in original). Plaintiff counters that Defendant "misunderstands the paragraph it cites, which emphasizes that the purity of the '237 Patent stocks is what distinguishes the claimed invention of the prior art." Pl.'s Resp. at 6.

Second, Defendant notes, *see* Def.'s Br. at 13–14, after the then-pending claims of the '237 patent were rejected for obviousness-type double patenting over claims 6, 8, 16, 20, 23, and 25 of the '650 patent and claims 1, 6, 10, and 11 of the '931 patent, *see* Lambert Decl. Ex. L at 602–03, both of which "provide[] methods and compositions for producing high titer, wild-type-free preparations of recombinant AAV ("rAAV") virions," *see* Lambert Decl. Ex. M at 610; Lambert Decl. Ex. N at 630, the Applicant filed a Terminal Disclaimer on May 1, 2001, thereby conceding that the '237 patent claims also are directed to rAAV virions. Def.'s Br. at 14 (citing Lambert Decl. Ex. C at 72–73). Plaintiff counters that "[t]here was no concession that the claims of the '237 Patent were limited to virions, as Genzyme argues. Rather, this was an acknowledgment of the fact that the claims of the '237 Patent require the stock to be free of detectable wild type AAV after 35 rounds of PCR." Pl.'s Resp. at 8.

Finally, Defendant explains, the then-pending claims of the '237 patent were also rejected as anticipated by Samulski, Lebkowski, and Shenk, *see* Lambert Decl. Ex. L at 603–06, with the Examiner characterizing the stock as consisting of "rAAV particles," *id.* at 605, which Defendant urges refers to rAAV virions. *See* Def.'s Br. at 14. Defendant notes that the Applicant's May 1, 2001 response indicated that "the stocks are substantially free of wild-type AAV and pseudo-wild-type AAV even when subjected to highly sensitive PCR testing methods that can detect 1 wild-type particle in 10^7, and preferably 10^9, recombinant particles." *See* Lambert Decl. Ex. C at 57. Because "the Applicant indicated to the Patent Office that the invention of the '237 patent is directed to recombinant AAV virions in order to have the patent allowed by the Patent Office[, t]he Applicant's statements (and those of the PTO) thus govern the claim scope." Def.'s Br. at 15. Plaintiff, however, again urges that "the similarities being referred to in the stocks of those references also related to the absence of wild-type contaminants, not the presence of virions." Pl.'s Resp. at 8.

"A patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution." *Univ. of Pittsburgh of Commonwealth Sys. of Higher Educ. v. Hedrick*, 573 F.3d 1290, 1297 (Fed. Cir. 2009). The Court must agree with Plaintiff that the explicit references to "virions" and "particles" above do not appear to amount to "clear and unmistakable" disavowals; nonetheless, they are "evidence of how the PTO and the inventor understood the patent." *Phillips*, 415 F.3d at 1317. That evidence conforms to Defendant's evidence from the '237 patent's claims themselves and specification, further bolstering Defendant's construction(s).

d. The Prior Art Cited in the '237 Patent

Finally, "prior art cited in a patent or cited in the prosecution history of the patent constitutes intrinsic evidence." *Kumar v. Ovonic Battery Co.*, 351 F.3d 1364, 1368 (Fed. Cir. 2003). Defendant argues that prior art explicitly cited in the '237 patent—specifically, the Shenk et al. patents, U.S. Patent Nos. 5,436,146 and 5,753,500 (the "'500 patent") and Samulski et al. publication, *Helper-Free Stocks of Recombinant Adeno-Associated*

Viruses: Normal Integration Does Not Require Viral Gene Expression, J. Virol. Vol. 63 No. 9 (1989)—show that "a stock of rAAV" has the same meaning as "a stock of rAAV virions." Def.'s Br. at 16.

Defendant first points to the Shenk patents. *See id.* The Inventor listed the Shenk patents under the "references cited" in the '237 patent. *See* Lambert Decl. Ex. A at 2. The Shenk patents define "helper-free virus stocks of recombinant AAV" as "stocks of recombinant AAV virions which contain no measurable quantities of wild-type AAV or undesirable recombinant AAV." Lambert Decl. Ex. E at 6:32–35; Lambert Decl. Ex. R at 6:9–12. In discussing the Technical Background of the '237 patent, the Inventor also discusses Shenk patent '500, of which the resultant rAAV stocks still contain unacceptable levels of AAV contaminants:

> Many attempts have been made to deal with the problem of pseudo-wild-type formation, all of which have failed. Most recently, Shenk et al. (US. Pat. No. 5,753,500) claimed to have achieved wild-type-free stocks of rAAV. The helper vector used, pAAV/Ad, was constructed with AAV rep and cap genes located between adenovirus inverted terminal repeats, and all of the AAV helper vector's sequences homologous to AAV vector sequences were removed. Several laboratories have reported, however, that the pAAV/Ad helper vector generates between 0.01 and 10% wild-type AAV. This level of contaminating AAV is unacceptable for human clinical trials.

'237 patent at 3:36–47. Defendant next points to the Samulski et al. publication, in which the authors appear to use the terms "recombinant AAV stocks" and "stocks of recombinant AAV virions" interchangeably. *See* Def.'s Br. at 16–17 (quoting Lambert Decl. Ex. F at 110).

Plaintiff counters that the Inventor of the '237 patent was not an inventor of the Shenk patents or an author to the Samulski publication, meaning that "those definitions do not reflect his understanding of those terms." ECF No. 100 at 3 (incorporated by Pl.'s Resp. at 8 n.3). Further, Plaintiff argues, the Shenk patents and Samulski publication are

/ / /

"technically distinct" from the '237 patent, *id.*, and the Inventor "repeatedly distinguished" the Shenk patents during prosecution. *Id.* at 3–4.

In construing asserted claims, courts may consider "prior art proffered by one of the parties, whether or not cited in the specification or the file history, . . . to demonstrate how a disputed term is used by those skilled in the art." *Vitronics*, 90 F.3d at 1584; *see also In re Cortright*, 165 F.3d 1353, 1358 (Fed. Cir. 1999) ("Prior art references may be 'indicative of what all those skilled in the art generally believe a certain claim term means.'") (quoting *Vitronics*, 90 F.3d at 1584). A claim term will not have its ordinary meaning "if the intrinsic evidence shows that the patentee distinguished that term from prior art on the basis of a particular embodiment." *CCS Fitness*, 288 F.3d at 1366–67. "When prior art that sheds light on the meaning of a term is cited by the patentee, it can have particular value as a guide to the proper construction of the term, because it may indicate not only the meaning of the term to persons skilled in the art, but also that the patentee intended to adopt that meaning." *Arthur A. Collins, Inc. v. N. Telecom Ltd.*, 216 F.3d 1042, 1045 (Fed Cir. 2000) (rejecting the district court's claim construction which "declined to consider the teachings of [prior art referenced in the patent] to ascertain the meaning" of a claim term).

In *Kumar*, the Federal Circuit found a prior art reference cited during the prosecution history of the patent at issue to be controlling where the prior art reference was "extensively discussed and distinguished" during the prosecution of the patent and "was considered by both the applicant and the examiner to be highly pertinent . . . , and there [wa]s no indication that the [prior art reference]'s express definition . . . was in any way at variance with the definition that would have been used by those skilled in the art at the time." 351 F.3d at 1367–68.

So too here. The Inventor notes in the '237 patent that the '500 patent "claimed to have achieved wild-type-free stocks of rAAV," but that "[s]everal laboratories have reported . . . that the [Shenk] helper vector generates between 0.01 and 10% wild-type AAV." '237 patent at 3:39–47. The Inventor then distinguishes his claimed stocks as a "significant advancement" over the Shenk stocks in terms of purity from pseudo-wild-type

AAV and efficiency of rAAV production. *See* '237 patent at 3:50–54. As Defendant notes, *see* Def.'s Br. at 16, the'500 patent claimed stocks of rAAV virions. *See* Lambert Decl. Ex. R at 6:9–12. The Inventor's citation to the'500 patent therefore would suggest that the Inventor himself viewed his stocks as stocks of rAAV virions.

The Shenk patents and Samulski publication were also discussed and distinguished extensively during the patent prosecution process, *see, e.g.*, Lambert Decl. Ex. C at 60–63; Lambert Decl. Ex. D at 77–80; Lambert Decl. Ex. L at 605; Lambert Decl. Ex. P at 657–59, an indication that the Examiner and Applicant considered them highly pertinent to the Invention claimed by the '237 patent. In comparing the stocks of the '237 invention to those claimed by Shenk, the Applicant noted that "these stocks have several orders of magnitude more recombinant virions than the prior stocks." Lambert Decl. Ex. C at 62. As Plaintiff itself concedes, *see supra* Section II.B.1.c, the Applicant distinguishes the Shenk patents on "the absence of wild-type contaminants, not the presence of virions." *See* Pl.'s Resp. at 8. The Shenk patents and Samulski publication therefore support Defendant's contention that the Applicant, the Examiner, and a person of ordinary skill in the art would have understood a stock of rAAV to mean a stock of rAAV virions in the context of the '237 patent.

Consequently, the intrinsic evidence as a whole supports Defendant's contention that the stocks claimed by the '237 patent are stocks of recombinant rAAV virions.

2. Defendant's Extrinsic Evidence

Defendant also relies on extrinsic evidence to support its contention that the term "a stock of recombinant AAV" means the same thing as "a stock of recombinant AAV virions." *See* Def.'s Br. at 17–19. Specifically, Defendant points to the testimony of its expert, Dr. Byrne, and Plaintiff's expert, Dr. Burger.[12] Dr. Byrne opines "that 'a stock of

[12] Defendant also cites to various extrinsic evidence supporting its contention that a "virion" is "an individual virus particle," including the 1995 and 2000 editions of *Molecular Cell Biology* by Harvey Lodish et al., Def.'s Br. at 17 (citing Lambert Decl. Ex. O), and the statements of Defendant's and Plaintiff's experts at the August 6, 2018 hearing on Defendant's motion for summary judgment, *see* Def.'s

recombinant adeno-associated virus' (or 'a stock of recombinant AAV') would be understood by a person of ordinary skill in the art to be ***a stock of recombinant AAV virions***." *Id.* at 18 (quoting Lambert Decl. Ex. K ("Byrne Decl.") at 496 ¶ 8). Defendant also quotes testimony from the November 15, 2017 deposition of Plaintiff's expert, Dr. Burger, in which he purportedly "unequivocally testified that the claims of the '237 patent claim recombinant AAV virions." *See id.* For example, in discussing the first sentence of the Abstract of the '237 patent, Dr. Burger agreed that "the claims of the '237 Patent provide for preparations of recombinant AAV virions." *See* Lambert Decl. Ex. B at 43:21–44:10. Dr. Burger also testified that claim 1 of the '237 patent claimed "a stock of recombinant adeno-associated virus, which is composed of virions" and "[v]arious impurities, both viral and nonviral." *Id.* at 45:23–46:23; *see also id.* at 54:2–25.

Plaintiff, however, now seeks to counter the testimony of Dr. Byrne and the prior testimony of Dr. Burger with a November 2018 expert declaration from Dr. Burger, in which he opines, "[b]ased upon [his] understanding of the[claim 1 description of a stock of rAAV 'vector' and not a stock of rAAV 'virions'], as a POSA as of the priority date of the '237 Patent, it would have been scientifically inaccurate to limit a stock of 'vector' to a stock of 'virions.'" Burger Decl. ¶ 56. Dr. Burger relies heavily on the claim's use of the term "packaged," *see id.* ¶¶ 62–64, and the specification's generic definition for "vector," *see id.* ¶¶ 57, 65, in opining that, "as a POSA as of the priority date of the '237 Patent, [he] would have understood that the reference to a stock of 'packaged' rAAV vector ***includes***—but is not limited to—a stock of rAAV virions." *Id.* ¶ 65 (emphasis in original).

Dr. Byne's and Dr. Burger's November 2017 testimony is consistent with the intrinsic evidence whereas, for the reasons discussed above, *see supra* Section II.B.1, the November 2018 opinions of Dr. Burger contradict not only his prior testimony, but also the intrinsic evidence. For example, even in his December 2018 deposition testimony,

---

Br. at 19 (citing Aug. 6, 2018 Tr. at 18, 27–28); however, Plaintiff does not appear to contest this point. *See, e.g.*, Pl.'s Br. at 21 ("[A] 'virion' refers to . . . a single, individual virus particle.").

Dr. Burger conceded that a stock of rAAV plasmids would not contain wild-type AAV virions or pseudo-wild-type AAV virions.[13] *See* Second Lambert Decl. Ex. U at 41:18–23. This would render superfluous the requirement in claim 1 that the claimed stock have an undetectable level of wild-type adeno-associated virus following 35 rounds of PCR. *See* '237 patent at 23:11–26. The Court therefore concludes that, on the whole, the extrinsic evidence supports Defendant's proposed construction(s). *See, e.g.*, *Sumitomo Dainippon Pharma Co. v. Emcure Pharm. Ltd.*, 887 F.3d 1153, 1160 (Fed. Cir. 2018) (affirming district court's rejection of expert testimony and references that were contrary to intrinsic evidence); *Elbit Sys. of Am., LLC v. Thales Visionix, Inc.*, 881 F.3d 1354, 1358 (Fed. Cir. 2018) (affirming Patent Trial and Appeal Board's determination that "expert's testimony was 'unsupported' and entitled to 'little weight' because he did not address or account for" a limitation in his opinion); *see also Vitronics Corp.*, 90 F.3d at 1583 ("Allowing the public record to be altered or changed by extrinsic evidence introduced at trial, such as expert testimony, would make this right meaningless.") (citing *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1578 (Fed. Cir. 1995)).

Consequently, considering the totality of the record before it, the Court concludes that the intrinsic and extrinsic evidence support Defendant's proposed construction(s) that the stock of rAAV claimed by the '237 patent is composed of virions.

3. The HSV-1 Exclusion

Because the Court concludes that the resultant stock claimed by the '237 patent is properly understood within the context of the '237 patent to be composed of virions, the HSV-1 exclusion is properly read into the resultant stock as well. *See* Def.'s Br. at 20–24.

The specification is explicit that a "recombinant AAV virion" (or "rAAV virion") "is produced in a suitable host cell comprising an AAV vector, AAV helper functions, and accessory functions." '237 patent at 8:26–28. The specification also clearly specifies that

[13] Again, to the extent that Plaintiff relies on Dr. Burger's subsequently "corrected" deposition testimony to refute this point, this testimony is unavailing. *See supra* note 8.

"[v]iral-based accessory functions can be derived from any of the known helper viruses such as adenovirus, herpesvirus (*other than herpes simplex virus type-1*) and vaccinia virus." '237 patent at 7:48–51 (emphasis added). The patent specification therefore teaches that rAAV virions are produced using, among other things, accessory functions, which explicitly cannot be derived from HSV-1.

This conclusion is bolstered by the prosecution history. As Defendant notes, "the original parent patent application, Application No. 08/510,790, which was filed on August 3, 1995 and issued as U.S. Patent No. 5,622,856 ('the '856 patent'), . . . ***expressly allowed*** the use of HSV-1-derived helper functions." Def.'s Br. at 23 (emphasis in original) (citing Lambert Decl. Ex. H at 319 ("Helper viruses which will find use with the present systems include the adenoviruses; herpesviruses such as herpes simplex virus types 1 and 2; and vaccinia viruses.")). Even if it does not rise to the level of a prosecution disavowal,[14] it certainly is telling that the HSV-1 exclusion was introduced when Dr. Colosi—the Inventor of the '237 patent—filed parent Application No. 09/107,708 on June 30, 1998, and that the HSV-1 exclusion ultimately was adopted into the '931, '650, and '237 patents. *See* Lambert Decl. Ex. K ("Byrne Report") at 508–11. *See, e.g.*, *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1290 (Fed. Cir. 2009) ("[T]he [prior, foreign patent] application establishes unequivocally that [the patentee] knew and could describe both Crystal A and Crystal B. [The patentee] could have retained the disclosure of Crystal B to support the broader claims of the . . . patent[-in-suit], but instead disclosed and claimed A alone.").

Given the Court's conclusion based on the intrinsic and extrinsic evidence before it that the claims of the '237 patent are directed to stocks of rAAV virions, the Court must

---

[14] The Court must agree with Plaintiff that the Applicant's inclusion that accessory functions are derived from "known helper viruses . . . other than HSV-1" in distinguishing the helper viruses of Colosi(A), Colosi(B), and Ferrari from the wild-type AAV-free stocks of the '237 patent, *see* Lambert Decl. Ex. C at 63, does not amount to a clear and unmistakable disclaimer of accessory functions derived from HSV-1. *See* Pl.'s Resp. at 10. Plaintiff is correct that the Applicant was not distinguishing these prior art references based on the HSV-1 exclusion, but rather on the basis that wild-type AAV is not properly classified as a helper virus.

also conclude from the available intrinsic evidence that those rAAV virions cannot be produced using accessory functions derived from HSV-1.

4. Plaintiff's Criticisms of Defendant's Proposed Construction

Plaintiff raises a number of arguments against Defendant's proposed construction(s) that the claimed stocks are limited to virions, *see* Pl.'s Br. at 17–25; Pl.'s Resp. at 2–9, that cannot be produced using accessory functions derived from HSV-1, *see* Pl.'s Br. at 24–25; Pl.'s Resp. at 9–10, which the Court addresses below.

a. Claim Differentiation

Plaintiff first argues Defendant's proposed construction ignores the tenant of claim differentiation. *See* Pl.'s Br. at 20–21. Under the doctrine of claim differentiation, each claim in a patent is presumptively different in scope. *Comark Comms., Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998). The doctrine provides the "presumption that an independent claim should not be construed as requiring a limitation added by a dependent claim." *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1380 (Fed. Cir. 2006); *see Phillips*, 415 F.3d at 1314–15 ("Differences among claims can also be a useful guide in understanding the meaning of particular claim terms. . . . For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim."). Claim differentiation, however, is not a "hard and fast rule of construction," and cannot be relied upon to "broaden claims beyond their correct scope." *Kraft Foods, Inc. v. Int'l Trading Co.*, 203 F.3d 1362, 1368 (Fed. Cir. 2000) (citations and quotation marks omitted).

Plaintiff argues that the use of the word "virion" in Claim 15 is "a compelling indicator . . . that the inventor deliberately chose ***not*** to use that word in claim 1." Pl.'s Br. at 20 (citing *Phillips*, 415 F.3d at 1314; *Ill. Tool Works, Inc. v. MOC Prods. Co.*, No. 09CV1887 JLS (MDD), 2011 WL 13100739, at *1 (S.D. Cal. May 12, 2011); ECF No. 86 at 17–18). Although Defendant agrees that virus and virion have different meanings, it contends that the doctrine of claim differentiation does not apply here because "the doctrine requires that the at-issue limitation 'is the only meaningful difference between the two

claims,'" whereas "Claim 1 says nothing about whether the virus is a 'pseudo-wild-type adeno-associated virus.'" ECF No. 87 at 8 (incorporated by Def.'s Resp. at 10) (quoting *Wenger Mfg., Inc. v. Coating Mach. Sys., Inc.*, 239 F.3d 1225, 1233 (Fed. Cir. 2001)).

In comparing claim 1 and claim 15, the Court does not read claim 15 to be referencing the disputed term at issue here. Claim 1 claims "[a] stock of recombinant adeno-associated virus free of wild-type adeno-associated virus," '237 patent at 23:11–12, whereas claim 15 claims "[t]he stock of claim 1, wherein said wild-type adeno-associated virus is a pseudo-wild-type adeno-associated virus virion." '237 patent at 24:55–57 (emphasis added). The reference to "said . . . virus" in claim 15 refers to "wild-type adeno-associated virus," not "[a] stock of recombinant adeno-associated virus." Consequently, dependent claim 15 does not give rise to a presumption that independent claim 1 cannot be read to include the word "virion" in the disputed phrase.

b. Composition Versus Product-by-Process Claims

Plaintiff also claims that "the prosecution history of the '237 Patent prohibits an interpretation of the claims of the '237 Patent as anything other than composition claims," but that "Genzyme's proposed construction would turn the claims of the '237 Patent into product-by-process claims." Pl.'s Br. at 22. In support of this position, Plaintiff cites an October 18, 2001 Amendment After Final Office Action, in which the Applicant purportedly "repeatedly confirmed that the claims were intended to be composition claims." *See id.* at 14 n.3. In particular, Plaintiff quotes from page 9, in which the Applicant wrote that, "[a]s explained in the interview, all of the pending claims pertain to stocks of recombinant AAV and are not directed to methods of use." *Id.* (quoting Declaration of April E. Weisbruch in Support of Supp. Br. ("Weisbruch Decl.," ECF No. 100-1) Ex. 4 at 9).

Defendant responds that this argument "is squarely contradicted by the prosecution history," Def.'s Resp. at 9, during which the Examiner characterized the claims as product-by-process claims. *See, e.g.*, Second Lambert Decl. Ex. W at 69 ("The instant claims are product by process claims."); Lambert Decl. Ex. D at 78 ("The instant claims are product

by process claims."). Defendant also contends that Plaintiff's citation to the prosecution history "is a red herring; the claims are not 'methods of use' claims, but they nonetheless contain process limitations." Def.'s Resp. at 10 (citing '237 patent claims 1–17; ECF No. 87 at 6; Aug. 6, 2018 Tr. at 58:3–12).

The Court must agree with Defendant. As discussed above, *see supra* Section II.B.1, the '237 patent clearly reveals that it claims stocks of rAAV, *see* '237 patent claims 1–17, produced by use of, among other things, novel nucleic acid molecules encoding AAV helper functions for rAAV production, *see, e.g.*, '237 patent Abstract; '237 patent at 3:60–61, and AAV helper function vectors. *See, e.g.*, '237 patent Abstract; '237 patent at 4:3–4. Despite the disputed characterization of the claims by the Application and the Examiner, the intrinsic evidence therefore supports construing the claims to include a process limitation. *See, e.g.*, *Medicines Co. v. Mylan, Inc.*, 853 F.3d 1296, 1304 (Fed. Cir. 2017) ("[This] decision does not impermissibly add a process limitation to a product claim that does not require a process because the specification's definition . . . itself injects a compounding process as a limitation in the asserted claims."); *Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1373 (Fed. Cir. 2007) ("[T]he pelletizing step is not just one possible method of manufacturing the products claimed in the Group II patents, but is an essential step in the process and thus a necessary limitation of the claims.").

c. Falsity of the HSV-1 Disclaimer

Finally, Plaintiff argues that the purported HSV-1 exclusion is "untrue as a matter of fact" because "it was known in the field at least as early as 1991 that HSV-1 could be used to produce rAAV virions." Pl.'s Br. at 24.

The Court must agree with Defendant that this argument is immaterial, *see, e.g.*, Def.'s Resp. at 10; ECF No. 87 at 7–8, as eloquently explained by Defendant's counsel at the August 6, 2019 hearing:

> For example, a patentee can have a patent on some furniture, and in it have a definition of table that says, "A table has four legs." MediciNova's position would be, "Hey, that's not right. That's incorrect. A table can have five legs, a table can have six legs."

> Or the patentee can say, "A table is a horizontal surface with three legs," . . . MediciNova's argument would be, "Hey, wait a minute, that's not right, therefore that exception can't apply." That is not the way lexicography works in a patent. The inventor can make a statement, an exception or a definitional statement, and that applies. You don't look at it and say, "Well, is that factually true?" It doesn't matter. The inventor says, "A table is a piece of wood with three legs," then that's the definition that's used in that patent.
>
> . . . That's the same situation here. The Inventor made a very clear statement of exclusion in the definition, reiterated it in the prosecution history, that's an exception. An argument that it's not true, that doesn't hold water because it doesn't have to be true. It just has to be something that the Inventor said applies in the patent, and that's what the Inventor did here.

Aug. 6, 2018 Tr. at 87:2–24.

Here, Dr. Colosi chose to define "accessory functions" to explicitly exclude those "derived from . . . herpes simplex virus type-1."[15] '237 patent at 7:41–51. Factually correct or not, that exclusion is dispositive. *See Phillips*, 415 F.3d at 1316 ("[O]ur cases recognize that the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs. . . . In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance as well, the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive.") (citation omitted).

The Court therefore adopts Defendant's proposed construction(s) of the term "[a] stock of recombinant adeno-associated virus" as being directed to virions and to which the

/ / /

---

[15] Dr. Colosi's motivation for including the HSV-1 exclusion—whether because of prior art, *see* Second Lambert Decl. Ex. S at 65:23–66:1, or because he believed (correctly or not) that the HSV-1-derived accessory functions were less efficient than others, *see* Lambert Decl. Ex. I at 4:45–56—is irrelevant. The main point is that Dr. Colosi did not include the HSV-1 exclusion "by error"; rather, the exclusion was explicitly added to the '237 patent during prosecution. *See supra* Section II.B.3.

express definitions for rAAV virion and accessory functions apply, thereby excluding stocks of rAAV made using accessory functions derived from HSV-1.

CONCLUSION

In light of the foregoing, the Court **DENIES** Plaintiff's Motion to Strike (ECF No. 130) and **ADOPTS** Defendant's proposed construction of the term "[a] stock of recombinant adeno-associated virus" in the '237 patent to mean "[a] stock of recombinant adeno-associated virus virions," to which the express definitions for "recombinant AAV virion" and "accessory functions" from the '237 patent apply, meaning that the stocks claimed by the '237 patent exclude stocks of rAAV made using accessory functions derived from the herpes simplex type-1 virus.

Within seven (7) days of the electronic docketing of this Order, the Parties **SHALL FILE** a Joint Status Report indicating their respective positions concerning the status of this action and proposing a joint schedule of pretrial dates.

IT IS SO ORDERED.

Dated: September 3, 2019

Janis L. Sammartino
Hon. Janis L. Sammartino
United States District Judge