

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

GENZYME CORPORATION and)	
AVENTIS INC.,)	
)	
Plaintiffs,)	
)	C.A. No. 21-1736 (RGA)
v.)	
)	JURY TRIAL DEMANDED
NOVARTIS GENE THERAPIES, INC.)	
and NOVARTIS PHARMACEUTICALS)	
CORPORATION,)	
)	
Defendants.)	

CLAIM CONSTRUCTION ORDER

In accordance with the Court’s August 18, 2023, Memorandum Opinion (D.I. 263) (“Mem. Op.”), the terms of U.S. Patent Nos. 6,596,535 (“the ’535 patent”), 7,125,717 (“the ’717 patent”), 7,785,888 (“the ’888 patent”), 7,846,729 (“the ’729 patent”), 8,093,054 (“the ’054 patent”), and 9,051,542 (“the ’542 patent”) are construed as set forth below:¹

TERM	PATENT CLAIMS	CONSTRUCTION
“AAV inverted terminal repeat (ITR) sequence”	’535 patent, claims 22-26, 28-29; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11- 13, 15, 17-27, 30-32, 34, 36.	“a term well-understood in the art, it is an approximately 145-nucleotide sequence that is present at both termini of the native single-stranded AAV genome. The outermost 125 nucleotides of the ITR can be present in either of two alternative orientations, leading to heterogeneity between different AAV genomes and between the two ends of a single AAV genome. The outermost 125 nucleotides also contains several shorter regions of self-complementarity, allowing

¹ Per the Court’s direction, the parties will meet and confer before trial regarding simplification of the claim constructions on which the parties had agreed. Mem. Op. at p. 4 n.2.

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		intrastrand base-pairing to occur within this portion of the ITR.”
“coding region” / “coding sequence”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 6-7, 9, 11-13, 15, 19-27, 30-32, 34, 36.	“for a polynucleotide, a sequence of contiguous nucleotides which gives rise in a host cell to a transcription and/or translation product”
“flank” / “flanking” / “flanked”	’535 patent, claims 3, 5, 8-11, 13, 15, 18-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9.	“situate(d) to the side of, although not necessarily directly adjacent to”
“helper function” / “helper virus function”	’535 patent, claims 22-26, 28, 29; ’729 patent, claims 1-5, 7-9.	“an activity that is required for replication and/or packaging of a parvovirus, such as AAV, but is not encoded within that parvovirus”
“helper virus”	’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claim 9; ’054 patent, claims 2, 18-27, 30-32, 34, 36.	“a virus that allows AAV (which is a defective parvovirus) to be replicated and packaged by a host cell”
“heterologous”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“derived from an entity that is genotypically distinct from an entity to which it is compared or into which it is introduced or incorporated. For purposes of this invention, ‘heterologous’ means heterologous with respect to a virus which is the basis of a recombinant viral vector. Accordingly, and as an example, an rAAV vector of the invention can be used to introduce and/or

TERM	PATENT CLAIMS	CONSTRUCTION
		express a mammalian, and thus ‘heterologous’ sequence, into a mammalian cell.”
“heterologous nucleotide sequence”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11- 13, 15, 17-27, 30-32, 34, 36.	“a nucleotide sequence derived from a genotypically distinct entity from that of the rest of the sequence to which it is compared or into which it is introduced or incorporated”
“heterologous sequence”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9.	“a heterologous polynucleotide sequence that can comprise a sequence of interest in gene therapy (such as a gene encoding a protein or RNA transcript, such as an antisense transcript or a ribozyme, of therapeutic interest) and/or a selectable or detectable marker”
“host cell”	’535 patent, claims 6-11, 22- 26, 28-29; ’729 patent, claims 1-5, 7-9.	“a cell which has been or can be a recipient for a vector or vectors of this invention and the progeny thereof”
“inverted terminal repeat” / “ITR sequence”	’535 patent, claims 3, 5, 8-11, 13, 15, 18-21; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6.	“a term well understood in the art and refers to relatively short sequences found at the termini of viral genomes which are in opposite orientation”
“most”	’535 patent, claims 2-5, 8-11, 13-15, 17-26, 28-29; ’717 patent, claims 3-6, 12-15; ’888 patent, claims 1-2, 4, 6; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“more than half”
“operably linked”	’054 patent, claims 11-13, 15, 30-32, 34.	“an arrangement of two or more components, wherein the components are in a relationship permitting them to function in a

TERM	PATENT CLAIMS	CONSTRUCTION
		coordinated manner. By way of illustration, a transcriptional regulatory sequence or a promoter is operably linked to a coding sequence if the transcriptional regulatory sequence or promoter facilitates some aspect of the transcription of the coding sequence.”
“polynucleotide”	’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 4, 6; ’054 patent, claims 7, 19-27, 30-32, 34, 36.	“a polymeric form of nucleotides of any length”
“promoter”	’054 patent, claims 11-13, 30-32.	“a nucleotide sequence that directs the transcription of a gene or coding sequence to which it is operably linked”
“recombinant”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 2, 12-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“A genetic entity distinct from that generally found in nature. As applied to a polynucleotide or gene, this means that the polynucleotide is the product of various combinations of cloning, restriction and/or ligation steps, and other procedures that result in the production of a construct that is distinct from a polynucleotide found in nature.”
“recombinant adeno-associated virus (rAAV)”	’535 patent, claims 12-15, 28; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1, 2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“an rAAV vector packaged into an AAV virus”
“region which forms intrastrand base pairs”/ “sequence forms intrastrand base	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6;	“a region (such as a coding region) which is complementary in sequence to another region in the same strand, and is thus capable of forming base pairs with

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pairs”/ “rAAV genome which forms intrastrand base pairs” / “nucleotide sequence can form intrastrand base pairs”	’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	the complementary sequence, i.e., is self-annealing”
“sequence complexity” / “complexity”	’535 patent, claims 2-3, 5, 8-11, 13-15, 17-26, 28-29; ’717 patent, claims 3-4, 12-13.	“the total amount of unique sequence present in a polynucleotide”
“vector”	’535 patent, claims 1-26, 28-29; ’717 patent, claims 1-8, 11-17, 20; ’888 patent, claims 1-2, 4, 6; ’729 patent, claims 1-5, 7-9; ’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“a recombinant plasmid or virus that comprises a polynucleotide to be delivered into a host cell, either in vitro or in vivo”
“filtration . . . through a 0.22 µm filter”	’542 patent, claim 6.	“passing a liquid through a 0.22 µm filter to remove materials”
“ionic strength”	’542 patent, claims 5, 6.	“one half of the sum of the molar concentration of each solute species times the square of the charge on each species for all excipients present in the solution (calculated according to the equation: $\mu = \frac{1}{2} \sum c_i z_i^2$)”
“multivalent ion”	’542 patent, claims 5, 6.	“an ionic species having a charge valency greater than one (whether positive or negative)”
“recombinant adeno-associated virus (AAV) vector particles” / “AAV vector particles” / “recombinant virus particles”	’542 patent, claims 5, 6.	“recombinant AAV virion or virus particles”
“A 5’ AAV inverted terminal	’054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	“A native 5’ AAV inverted terminal repeat (ITR) sequence . .

TERM	PATENT CLAIMS	CONSTRUCTION
repeat (ITR) sequence, a first heterologous nucleotide sequence, an internal AAV ITR sequence, a second heterologous nucleotide sequence, and a 3' AAV ITR sequence"		. a native internal AAV ITR sequence . . . and a native 3' AAV ITR sequence."
"recombinant AAV vector (rAAV vector)"	'888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9; '535 patent, claims 1-26, 28-29; '717 patent, claims 1-8, 11-17, 20. ²	"a polynucleotide vector comprising one or more heterologous sequences that are flanked by at least one AAV ITR sequence wherein each ITR of the polynucleotide vector is a native AAV ITR sequence."
"rAAV vector genome" / "rAAV genome"	'888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9; '054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36. ³	"the genetic material of a recombinant AAV vector"
"along most or all of its length" / "along its length"	'535 patent, claims 2-5, 8-11, 13-15, 17-26, 28-29; '717 patent, claims 3-6, 12-15; '888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9; '054 patent, claims 1-7, 9, 11-13, 15, 17-27, 30-32, 34, 36.	Plain and ordinary meaning
"conditions that allow" / "conditions which allow"	'535 patent, claims 22-26, 28-29; '717 patent, claims 1-8, 11-17, 20;	Plain and ordinary meaning

² The identification of patent claims has been corrected consistent with the parties' understanding of the Court's intent based on the parties' Joint Claim Construction Brief (D.I. 101.)

³ See *supra* fn. 1.

TERM	PATENT CLAIMS	CONSTRUCTION
	'729 patent, claims 1-5, 7-9; '054 patent, claims 18-27, 30-32, 34, 36.	
“Forms intrastrand base pairs such that expression of a coding region of [a] heterologous sequence is enhanced relative to a second rAAV vector that lacks sufficient intrastrand base pairing to enhance said expression” ⁴	'535 patent, claims 1-26, 28-29; '717 patent, claims 1-8, 11-17, 20; '888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9.	Indefinite
“dynamic light scattering”	'542 patent, claim 5.	“a technique in physics that can be used to determine a size distribution profile of small particles in suspension or polymers in solution”
“purified”	'542 patent, claims 5, 6.	“having been subjected to a purification procedure”
“significant aggregation”	'542 patent, claims 5, 6.	Plain and ordinary meaning
“storage” / “stored”	'542 patent, claims 5, 6.	“maintenance in a frozen or non-frozen state”

⁴ There is some variation in the actual language of this term in the claims of the different patents, but these variations do not affect the Court’s determination. Mem. Op. at p. 15 n.5. The Court does not address the isolated terms “enhance” or “enhanced” as used in the '535 patent, claims 1-26, 28-29; '717 patent, claims 1-8, 11-17, 20; '888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9, because the instant, longer term is determined to be indefinite. Mem. Op. at p. 15.

In light of these constructions, the following patent claims have been determined to contain an indefinite claim term and are therefore invalid: '535 patent, claims 1-26, 28-29; '717 patent, claims 1-8, 11-17, 20; '888 patent, claims 1-2, 4, 6; '729 patent, claims 1-5, 7-9.

IT IS SO ORDERED this 30 day of August, 2023.

/s/ Richard G. Andrews

United States District Court Judge