NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IMMUNOMEDICS, INC., Plaintiff, v. ROGER WILLIAMS MEDICAL CENTER, *et al.*, Defendant.	Civil Action No.: 15-4526 (JLL) **OPINION**

LINARES, District Judge.

This matter comes before the Court by way of an application for claim construction by Plaintiff Immunomedics, Inc. and Defendants Dr. Richard P. Junghans, Dr. Steven C. Katz and Roger Williams' Medical Center. While this patent infringement action involves three separate patents, the parties only seek construction of certain language contained in claims 1, 14, and 23 of United States Patent No. 6,676,924 ("'924 patent") and claims 1 and 4 of United States Patent No. 6,926,893 ("'893 patent") (collectively, the "patents-in-suit").[1] The Court has considered the parties' written submissions (ECF Nos. 52, 63, 64, 98, 99) and the oral arguments advanced at the *Markman* hearing which was held on January 23, 2017. (ECF No. 123).

[1] The third patent-in-suit bears United States Patent No. 5,874,540 and does not contain the disputed term. Accordingly, the said patent will not be discussed herein.

I. BACKGROUND

A. The Patents

The subject patents deal with, and relate to, the treatment of cancer and other infectious diseases by utilizing specific antibodies to seek out and destroy the afflicted cells. (*See* Markman Transcript at 7:25-9:16).[2] The patents-in-suit claim a specific method of treating said illnesses by utilizing a humanized antibody along with Chimeric Antigen Receptor T Cells ("CAR-T Technology"). (*See* ECF Nos. 77-2, 77-2). To employ this method, Plaintiff "generated a DNA that calls for [a specific antibody known as] humanized MN-14." (Trans. at 13:24-25). Plaintiff then asserts that humanized MN-14 ("hMN-14") can be put into "viral vectors." (Trans. at 14:1-2). A viral vector is a virus that can place new DNA into a cell; and in this case, specifically a T Cell. (Trans at 8:14-17). Thereafter, the cell will generate hMN-14 on the surface. (Trans. at 14:2-3). Once this happens, the hMN-14 binds itself to the tumor and will destroy the cancer cell. (Trans at 14:3-5).

The '924 Patent claims a "method for treating a patient comprising administering a conjugate to said patient in an effective amount for treatment." (*See* ECF No. 77-2 at 46, claim 1; Trans. at 23:24-24:1). The conjugate here would include a conjugate of hMN-14 and a T Cell. (Trans. at 24:1-3). Said differently, the '924 Patent claims methods treating or diagnosing patients compromising administering a therapeutic or diagnostic agent bound to hMN-14. (*See* ECF No. 77 ("Compl.") ¶¶ 189-90).

Plaintiff's '893 Patent claims a "method for inducing a cellular immune response in a patient against a tumor that expresses carcinoembryonic antigen (CEA), said method comprising: administering an effective immunostimulatory amount of transferred T cells to a patient; and

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[2] The Transcript from the January 23, 2017 *Markman* Hearing shall be cited as "Trans." followed by the page and line numbers, separated by a colon.

subsequently administering at least one cytokine to said patient." (ECF No. 77-3 at 11, claim 1). "[T]he '893 Patent talks about an effective amount of an effective immunostimulatory amount of transfected T Cells to a patient." (Trans. at 44:20-22). Thus, the '893 Patent claims methods for introducing cellular immune response against a tumor that expressed CEA. (Compl. ¶¶ 202-03).

B. Disputed Term and Proposed Construction

The parties have asked the Court to construe the term "effective amount." "Effective amount" is used three times in the '924 Patent and twice in the '893 Patent. In the '924 Patent "effective amount" appears in Claims 1, 14 and 23. (ECF No. 77-2 at 46-48). Claim 1 of the '924 claims

> A method for treating a patient comprising administrating a conjugate to said patient *in an effective amount* for treatment, wherein said conjugate comprises:
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> > a therapeutic agent bound to a humanized Class III, anti-CEA, monoclonal antibody (mAb) or a fragment thereof, wherein complementarily-determining regions (CDRs) of said humanized mAb are CDRs from a parental murine Class III, anti CEA mAb, wherein the light chain variable region comprises CDRL1 comprising KASQDVGTSA (SEQ ID NO:20), CDRL2 comprising WTSTRHT (SEQ ID NO: 21), and CDRL3 comprising QQYSLYRS (SEQ ID NO:22), and the heavy chain variable region comprises CDRH1 comprising TYWMS (SEQ ID NO:23), CDRH2 comprising EIHPDSSTINYAPSLKD (SEQ ID NO:24), and CDRH3 comprising LYFGFPWFAY (SEQ ID NO:25), and each of the framework regions (FRs) of the light and heavy chain variable regions is from a human antibody, where said humanized mAb retains the binding specificity of said parental murine Class III, anti-CEA mAb.

(ECF No. 77-2 at 46)(emphasis added). Next, Claim 14 claims

> A method for diagnosing a patient comprising administering a conjugate to said patient *in an effective amount* for diagnosis, wherein said conjugate comprises:
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> > a diagnostic agent bound to a humanized Class III, 30 anti-CEA, monoclonal antibody (mAb) or a fragment thereof, wherein the complementarity-determining regions (CDRs)

> of said humanized mAb are CDRs from a parental murine Class III, anti-CEA mAb, wherein the light chain variable region comprises 35 CDRLl comprising KASQDVGTSVA (SEQ ID N0:20), CDRL2 comprising WTSTRHT (SEQ ID N0:21), and CDRL3 comprising QQYSLYRS (SEQ ID N0:22), and the heavy chain variable region comprises CDRH1 comprising TYWMS (SEQ ID N0:23), 40 CDRH2 comprising EIHPDSSTINYAPSLKD (SEQ ID N0:24) and CDRH3 comprising LYFGFPWFAY (SEQ ID N0:25), and each of the framework regions (FRs) of the light and heavy chain variable regions is from a human antibody, wherein said humanized mAb 45 retains the binding specificity of said parental murine Class III, anti-CEA mAb.

(ECF No. 77-2 at 47). Finally, Claim 23 claims

> A method for treating a patient comprising administering a humanized Class III, anti-CEA, monoclonal antibody (mAb) to said patient *in an effective amount* for treatment, wherein said mAb comprises:
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> > a humanized Class III, anti-CEA, monoclonal antibody (mAb), wherein the complementarity-determining regions (CDRs) of said humanized mAb are CDRs from a parental murine Class III, anti-CEA mAb or a fragment thereof, wherein the light chain variable region comprises CDRL1 comprising KASQDVGTSVA (SEQ ID N0:20), CDRL2 comprising WTSTRHT (SEQ ID N0:21), and CDRL3 comprising QQYSLYRS (SEQ ID N0:22), and the heavy chain variable region comprises CDRH1 comprising TYWMS (SEQ.ID) N0:23), CDRH2 comprising EIHPDSSTINYAPSLKD (SEQ ID N0:24) and CDRH3 comprising LYFGFPWFAY (SEQ ID N0:25), and each of the framework regions (FRs) of the light and heavy FRH4 comprises a region of 9-13 amino acids that occurs naturally in the FRH4 of a human antibody.

(ECF No. 77-2 at 47-48)(emphasis added).

The '893 Patent utilizes the term "effective" in Claims 1 and 4. (ECF No. 77-3). Claim 1 of the '893 patent claims

> A method for inducing a cellular immune response in a patient against a tumor that expresses carcinoembryonic antigen (CEA), said method comprising:
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> > administering an *effective immunostimulatory amount* of transfected T cells to a patient; and subsequently administering at least one cytokine to said patient; wherein

> said transfected T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells; wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable regions of a Class III anti-CEA antibody, wherein the Class III anti-CEA antibody is MN-14 or humanized MN-14, and further wherein the variable regions of the α and β polypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.

(ECF No. 77-3 at 11)(emphasis added).

Claim 4 of the '893 patent claims

> A method for inducing a cellular immune response in a patient against a tumor that expresses carcinoembryonic antigen (CEA), said method comprising:
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> > administering *an effective immunostimulatory amount* of transfected T cells to a patient; and subsequently administering at least one cytokine to said patient; wherein said T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells; wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable regions of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody, wherein the anti-idiotype antibody is WI2, and further wherein the variable regions of the C. and f polypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.

(ECF No. 77-3 at 11)(emphasis added). The parties agree that the term "immunostimulatory" contained in Claim 1 of the '893 Patent is not subject to construction and that the only term that the Court needs to construe in this claim is "effective amount." (Trans. at 25:24-26:5).

Plaintiff proposes that this Court decline to construe the disputed term because Defendants cannot show that the term is indefinite, or, in the alternative, construe it as having its plain and ordinary meaning. (*See* ECF No. 64 ("Pl. Open. Br.") at 13; ECF No. 98 ("Pl. Rep. Br.") at 10). Moreover, Plaintiff asserts that, should the Court decline to construe the term as having its plain and ordinary meaning, that the Court should construe "effective amount" and "effective immunostimulatory amount" to mean "an amount capable of producing [the claimed] result." (Trans. at 28:25-29:2). Defendants do not propose a construction. Rather, Defendants aver that the disputed term is indefinite and the patents-in-suit are therefore invalid. (ECF No. 63 ("Def. Open. Br.") at 6-10); (ECF No. 99 ("Def. Rep. Br.") at 10).

II. LEGAL STANDARD

A court's analysis of a patent infringement claim is two-fold. *Tate Access Floors, Inc. v. Interface Architectural Resources, Inc.*, 279 F.3d 1357, 1365 (Fed. Cir. 2002). The court must first define the meaning and scope of the patent claims as a matter of law. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 978 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). The court then engages in a comparison of the claims as construed to the alleged infringing product or method. *Tate*, 279 F.3d at 1365. At this stage, the Court must only engage in the first step.

Claim construction is a matter of law to be determined solely by the court. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005), *cert. denied*, 546 U.S. 1170 (2006). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Id.* at 1312 (quotations omitted). In construing the terms of a patent, a court should look first to the language of the claim itself. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). The terms in the claim "are generally given their ordinary and customary meaning." *Id.* at 1582. "[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*, 415 F.3d at 1313. A court "must look at the ordinary meaning in the context of the written description and the prosecution history." *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1319 (Fed. Cir. 2005). The court should turn 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).

To this end, the court should first examine the intrinsic record—the patent itself, including the claims, the specification and, if in evidence, the prosecution history. *Vitronics*, 90 F.3d at 1582 (citing *Markman*, 52 F.3d at 979). The specification "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." *Id.* Indeed, the Federal Circuit has explained that the specification is "'usually . . . dispositive . . . [and] the single best guide the meaning of a disputed term.'" *Phillips*, 415 F.3d at 1315 (quoting *Vitronics*, 90 F.3d at 1582). 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." *Id.* at 1317. The specification is also an important guide in claims construction as it may contain "an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* at 1316.

Additionally, the court should consult the patent's prosecution history as it "provides evidence of how the PTO and the inventor understood the patent." *Id.* Courts should be circumspect in reviewing a prosecution history as it represents "an ongoing negotiation between the PTO and the applicant, rather than the final product of the negotiation." *Id.* A district court may also examine extrinsic evidence: "all evidence external to the patent and prosecution history." *Markman*, 52 F.3d at 980; *Phillips*, 415 F.3d at 1317-18 (stating that the Federal Circuit "ha[s] authorized district courts to rely on extrinsic evidence"). Such evidence consists of testimony by the inventor or by experts, dictionaries, and treatises. *Markman*, 52 F.3d at 980. In particular, a

court may find reference to technical dictionaries useful "in determining the meaning of particular terminology." *See Phillips*, 415 F.3d at 1318. However, extrinsic evidence is generally thought to be less reliable than the patent and prosecution history, *id.* at 1318-19; in essence, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language," *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)(quotation omitted). With this framework in mind, the Court now turns to the disputed claim language.

Finally, a party may challenge the definiteness of the disputed term. Should the Court find the term indefinite the claim is rendered invalid. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2124-25 (2014). "A lack of definiteness renders invalid 'the patent or any claim in suit.'" *Nautilus*, 134 S.Ct. at 2125 (quoting 35 U.S.C. § 282, ¶2(3)). The Federal Circuit recently confirmed that an "[i]ndefiniteness [defense] must be proven by clear and convincing evidence." *Sonix Tech. Co., Ltd. V. Publications Int'l, Ltd.*, --- F.3d ----, *5 (Fed. Cir. 2017). The "indefiniteness analysis involves general claim construction principles." *Sonix*, --- F.3d ---- at *6 (citing *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325, 1332 (Fed. Cir. 2010).

III. ANALYSIS

As noted, Defendants have advanced an indefiniteness defense. Accordingly, the Court will address this argument first. The term "effective amount" is used in Claims 1, 14 and 23 of the '924 Patent, and "effective immunostimulatory amount" is used in Claims 1 and 4 of the '893 Patent. As discussed, neither party disputes the meaning of the term "immunostimulatory," and agree that this term means to cause a person's immune system to have a reaction. (Trans. at 25:24-26:5). Thus, the only question before the Court is the meaning of "effective term" as it appears in the aforementioned patents.

Here, the Court finds that, based on both intrinsic and extrinsic evidence, the term "effective amount" is not indefinite in either patent. The '924 Patents' specification provides clear guidance with regards to the term "effective amount." There, the specification explains that "for purpose of therapy, a humanized antibody conjugate and pharmaceutically acceptable carrier *are administered to a patient in a therapeutically effective amount.*" (ECF No. 77-2 at col. 10, ll. 53-56)(emphasis added). The specification goes on to explain that "[a] combination of a conjugate and pharmaceutically accepted carrier is said to be administered in a 'therapeutically effective amount' *if the amount administered is physiologically significant.*" (Id. at col. 10, ll. 53-59)(emphasis added). According to the specification "[a]n agent is 'physiologically significant' if its presence results in a detectable change in the physiology of a receipt patient." (Id. at col. 10, ll. 59-61)(emphasis added). The specification also explains that "[a] targeted therapeutic agent is 'therapeutically effective' if it delivers a higher proportion of the administered dose to the intended target that accretes at the target upon systemic administration of the equivalent untargeted agent." (Id. at col. 10, ll. 61-65). Accordingly, the '924 Patent's specification contains a clear definition and "acts as a dictionary [because] it expressly defines terms used in the claims." *Vitronics*, 90 F.3d at 1582.

Similarly, the term is not indefinite in the '893 Patent. Once again, the '893 Patent's specification contains a detailed definition for "therapeutically effective amount." The specification explains that, "[f]or purposes of therapy, antibodies or fragments are administered to a mammal in a *therapeutically effective amount.*" (ECF No. 77-3, col. 13, ll. 43-45)(emphasis added). "An antibody preparation is said to be administered in a '*therapeutically effective amount*' *if the amount administered is physiologically significant.* (ECF No. 77-3, col. 13, ll. 45-

47)(emphasis added). The specification further explains that "[*a*]*n agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient mammal.*" (ECF No. 77-3, col. 13, ll. 47-49)(emphasis added). Finally, the specification states that, "[i]n particular, *an antibody preparation of the present invention is physiologically significant if its presence invokes a humoral and/or cellular immune response in the recipient mammal.*" (ECF No. 77-3, col. 13, ll. 49-52)(emphasis added). Once again, the Court finds that the term is not indefinite. The specification of the '893 Patent contains a clear definition of what the term "effective amount" means in the context of the invention.

Moreover, extrinsic evidence also shows that "effective amount," as used in both the '924 and '893 Patents, is not indefinite. Specifically, Defendants themselves have used the term "effective" in various publications. (Trans. 33:15-22). Plaintiff points to two articles authored by Defendants Junghans and Katz wherein the subject technology is discussed and "effective" or "efficacious" was utilized regarding said technology. In December 2008, Defendant Junghans regarding the CEA technology. (*See* ECF No. 64-4 (*RP Junghans, et al., Clinical Cancer Research 2008 December 15; 14(24): 8112-8122*)). The purpose of the "report [was to] describe[] the development and preclinical qualification tests of 2nd generation (gen) anti-carcinoembryonic (CEA) designer T Cells for use in human trial." (Id. at 1). The report details the various tests conducted and the results of said tests. (Id.). In the results section, Defendant Junghans and his coauthors conclude that "2nd generation T cells were *more effective in suppressing tumor in animal models.*" (Id.)(emphasis added). Hence, it is apparent that Defendant Junghans, a person of ordinary skill in the art, has a clear understanding of the term "effective" as used in the context of the patents-in-suit.

Defendant Katz also has an understanding of the term, as he too has coauthored literature relating to the patents-in-suit. (ECF No. 64-5 (*SC Katz, RP Junghans, et al. Cancer Gene Therapy 2016 23, 142-48*)). The article begins by noting that "[m]etastatic spread of colorectal cancer (CRC) to the peritoneal cavity is common and difficult to treat, with many patients dying from malignant bowel obstruction." (Id. at 1). Defendant Katz and Junghans, along with their other coauthors, explain that they "are now studying intraperitoneal (IP) delivery of CAR-Ts for peritoneal carcinomatosis." (Id.). The article continues by stating that Defendants "have tested a novel pre-clinical strategy for regional IP CAR-T delivery combined with the targeting of suppressor cell populations in a murine model of PC." (Id.). Defendants further note that they "performed *in vivo* testing of IP CAR-T infusions in combination with suppressor cell depletion or blockade" and that, after 14 days, "*CAR-Ts alone significantly diminished the tumor burden* when compared with untreated mice." (Id. at 4)(emphasis added). Thereafter, Defendants conclude that "[t]he combination of CAR-Ts and anti-Gr-1 *was the most efficacious overall*" since "[o]n day 14, *there was no detectable tumor found* in any mouse that received the IP CAR-T." (Id.)(emphasis added). Therefore, it is apparent that both Defendants Katz and Junghans have an explicit understanding of the term "effective amount" as it pertains to the patents-in-suit.

In conclusion, the Court finds that the term "effective amount" is not indefinite. The specification of both patents continues an unambiguous definition of the term as it is used therein. Moreover, both Defendants, who are extremely familiar with the subject technology, use the term in their own scholarly articles and manuscripts. Defendants have failed to carry their burden in showing that the term in dispute is indefinite by clear and convincing evidence. Thus, the term

"effective amount," as used in the patents-in-suit, is not indefinite since a person of ordinary skill in the art would have an obvious understanding of same.

Furthermore, the Court finds that the term "effective amount" should be given its plain and ordinary meaning which, in the context of the patents-in-suit, is consistent with Plaintiff's proposed construction. As discussed, Defendants have not submitted any proposed construction that is different and only argue that the term is indefinite. The Court is cognizant that the Federal Circuit has held that where "the plain and ordinary meaning of the disputed claim language is clear, the district court [does] not err by declining to construe the claim term," *Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1291 (Fed. Cir. 2015), in the case at bar, although the Court does find that the term at issue has a plain and ordinary meaning, it also finds that the plain and ordinary meaning coincides with Plaintiff's proposed construction of "an amount capable of producing the claimed result," and hereby construes the term as such.

CONCLUSION

For the aforementioned reasons, this Court concludes that the term "effective amount" is not indefinite and construes it to mean "an amount capable of producing the claimed result."

DATED: February 28, 2017

JOSE L. LINARES
UNITED STATES DISTRICT JUDGE