IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VYTACERA BIO, LLC,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action No. 20-333-LPS-CJB
	)	
CYTOMX THERAPEUTICS, INC.,	)	
	)	
Defendant.	)	

REPORT AND RECOMMENDATION

In this patent infringement action filed by Plaintiff Vytacera Bio, LLC ("Plaintiff" or "Vytacera") against Defendant CytomX Therapeutics, Inc. ("Defendant" or "CytomX"), presently before the Court is the matter of claim construction. (D.I. 102; D.I. 103) The Court recommends that the District Court adopt the constructions set forth below.

I. BACKGROUND

A. Procedural Background

On March 4, 2020, Vytacera filed the instant action against CytomX in this Court. (D.I. 1) There are two patents-in-suit: United States Patent Nos. 8,809,504 (the "'504 patent") and 9,775,913 (the "'913 patent" and collectively with the '504 patent, the "patents-in-suit"). (*See* D.I. 1) United States District Judge Leonard P. Stark has referred this case to the Court to resolve all pre-trial matters, up to and including the end of fact discovery (including the resolution of claim construction proceedings). (D.I. 36)

Briefing with regard to claim construction was completed on July 9, 2021. (D.I. 58; D.I. 61) The Court conducted a *Markman* hearing by video conference on August 23, 2021 (hereinafter, "Tr.").

B. Factual Background

Vytacera is a Delaware corporation with its principal place of business in Portola Valley, California, (D.I. 1 at ¶ 2), and it owns the rights to the '504 patent and the '913 patent, (*id.* at ¶¶ 25, 32). CytomX is a Delaware corporation with its principal place of business in San Francisco, California. (*Id*. at ¶ 3) It is a clinical-stage biopharmaceutical company that specializes in cancer treatments, namely Probody® therapeutics. (*Id*.; D.I. 51 at 4) CytomX uses its Probody technology platform to conduct basic research and identify and develop certain pharmaceutical compounds. (D.I. 1 at ¶ 3)

Both of the patents-in-suit "relate[] to inhibitors that bind, inhibit, suppress, neutralize[] or decrease activity of a biologically active agent." (D.I. 1, ex. 1 (hereinafter, "'504 patent") Abstract; *id.*, ex. 2 (hereinafter, "'913 patent"), Abstract) The '504 patent is entitled "Inhibitor Which Is Deactivatable by a Reagent Produced by a Target Cell" and it issued on August 19, 2014. ('504 patent) The '913 patent is entitled "Method of Site Specific Activation of an Antibody by a Protease" and it issued on October 3, 2017. ('913 patent) In essence, the '504 patent teaches specifics regarding the composition of the inhibitors that reduce the activity of a biologically active agent, and the '913 patent teaches methods of their use. (D.I. 53 at 2; *see also* '504 patent, col. 3:50-52)[1] These inhibitors can be "deactivated by an enzyme produced by vertebrate cells" at the disease site, so that the biologically active agent is then released at the site in an active form, such that it can have a therapeutic effect for a patient. (*Id*., col. 3:52-64) Both patented inventions "can be used for treatment of a disease such as cancer, inflammatory[] or an autoimmune disease." (*Id*., col. 3:53-55)

Further details concerning the patents-in-suit will be addressed below in Section III.

[1] The patents-in-suit share a specification, (D.I. 51 at 1 n.1), so unless otherwise noted, when referring to the patents' specifications, the Court will simply cite to the '504 patent.

II. STANDARD OF REVIEW

It is well-understood that "[a] claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention." *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc*., 868 F.2d 1251, 1257 (Fed. Cir. 1989). Claim construction is a generally a question of law, although subsidiary fact finding is sometimes necessary. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 325-26 (2015).

The Court should typically assign claim terms their "'ordinary and customary meaning[,]'" which is "the meaning that the term[s] 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, 1312-13 (Fed. Cir. 2005) (citations omitted). However, when determining the ordinary meaning of claim terms, the Court should not extract and isolate those terms from the context of the patent; rather it should endeavor to reflect their "meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321; *see also Eon Corp. IP Holdings LLC v. Silver Spring Networks, Inc.*, 815 F.3d 1314, 1320 (Fed. Cir. 2016).

In proceeding with claim construction, the Court should look first and foremost to the language of the claims themselves, because "[i]t 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." *Phillips*, 415 F.3d at 1312 (internal quotation marks and citations omitted). For example, the context in which a term is used in a claim may be "highly instructive." *Id.* at 1314. In addition, "[o]ther claims of the patent in question, both asserted and unasserted, can . . . be valuable" in discerning the meaning of a particular claim term. *Id.* This is "[b]ecause claim terms are

normally used consistently throughout the patent, [and so] the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Moreover, "[d]ifferences among claims can also be a useful guide[,]" as when "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." *Id.* at 1314-15.

In addition to the words of the claims, the Court should look to other intrinsic evidence. For example, the Court should analyze the patent specification, which "may reveal a special definition given to a claim term . . . that differs from the meaning [that term] would otherwise possess" or may reveal an intentional disclaimer of claim scope. *Id.* at 1316. Even if the specification does not contain such revelations, it "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (internal quotation marks and citation omitted). That said, however, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). And a court should also consider the patent's prosecution history, if it is in evidence, because it "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution[.]" *Phillips*, 415 F.3d at 1317.

Extrinsic evidence, "including expert and inventor testimony, dictionaries, and learned treatises[,]" can also "shed useful light on the relevant art[.]" *Id.* (internal quotation marks and citations omitted). Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* (internal

quotation marks and citations omitted); *accord Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 981 (Fed. Cir. 1995).

In utilizing these resources during claim construction, courts should keep in mind that "[t]he 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." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998).

III. DISCUSSION

In their briefing, the parties raised disputes about five different claim terms. The Court subsequently ordered that resolution of the parties' dispute as to one term ("recognition domain") would be deferred to a later stage of the case, because the parties' briefing did not really get to the heart of the real dispute as to that term.[2] (*See* Tr. at 238-39; *see also* D.I. 94; D.I. 106) Below, then, the Court will recommend constructions for the four terms that are ready for resolution now.

A. "inhibitor"

The first disputed term, "inhibitor," appears, *inter alia*, in claim 1 of the '504 patent, and claims 1 and 22 of the '913 patent. Claim 1 of the '504 patent is representative for our purposes, and is reproduced below:

> **1**. An *inhibitor* which is deactivatable by a reagent produced by a target cell comprising:
>
> > (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of a biologically active agent wherein said first moiety is operably linked to;

[2] By the end of the *Markman* hearing, it seemed possible that the parties, now that they understood the other side's actual position as to the "recognition domain" term, might be able to come to agreement on a construction. The Court ordered the parties to further meet and confer on the issue. The parties did so, but were unable to agree. (D.I. 94)

(b) a second moiety specifically cleavable by a protease produced by a target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding activity of said *inhibitor*.

('504 patent, col. 83:11-20 (emphasis added)) The parties' proposed constructions are below:

Term	**Vytacera's Proposal**	**CytomX's Proposal**
"inhibitor"	"a first and second moiety as defined by the claim"	"a molecule, separate from the [biologically active agent/antibody], having the ability to bind, inhibit, suppress, neutralize, or decrease activity of a [biologically active agent/antibody]"

(D.I. 43 at 6; *see also* D.I. 51 at 6 & n.3)[3]

There is no dispute that there can be some type of connection (e.g., binding) between the claimed inhibitor and the biologically active agent. (Tr. at 37-38) But the crux of the parties' dispute is about whether the inhibitor can ever be a part of the *same molecule* as (i.e., be "chemically link[ed]" or "chemically attached" in the same molecule with regard to) the biologically active agent. *See id.* CytomX says it cannot, and that the inhibitor and the biologically active agent must always be separate molecules; Vytacera disagrees and says that the inhibitor and the biologically active agent can be a part of the same molecule. (D.I. 51 at 7; D.I. 53 at 8; Tr. at 16, 19, 21-27, 33-35) For the following two reasons, the Court agrees with CytomX.

[3] The '913 patent's claims state that the biologically active agent referenced therein is an "antibody," and so CytomX's construction is to be read as reciting "antibody" instead of "biologically active agent" with regard to those patent's claims. (D.I. 51 at 6 n.3)

First, the claim language provides strong indication that an "inhibitor" and a biologically active agent are separate entities that are not chemically attached. More specifically:

- The '504 patent claims state that the "inhibitor" interacts with a "biologically active agent," ('504 patent, col. 83:11-14), and the '913 patent claims state that the "inhibitor" interacts with an "antibody" (which the parties agree is a biologically active agent), ('913 patent, cols. 85:21-26, 86:56-60, 87:7-16; *see also* Tr. at 30, 45). By using different words for these two terms, the claims suggest that an "inhibitor" is a separate and distinct entity from a "biologically active agent."

- This is also indicated by the reality that the inhibitor has a component that takes action (i.e., "binds, inhibits, suppresses, neutralizes, or decreases activity of") that in turn affects the biologically active agent. It is hard to conceive of how a first entity (the inhibitor) could be said to "inhibit" or "suppress" or "neutralize" a second entity (the biologically active agent), if those two things were actually all part of the same chemical molecule. Put another way (as CytomX noted in its briefing), it seems nonsensical that the inhibitor could be part of the same molecule of the very thing that it inhibits. (*Cf.* D.I. 51 at 9 ("A unitary molecule that has one region that acts to inhibit another region that is the biologically active agent being inhibited[] would not *function* as an inhibitor.") (emphasis in original); *see also* Tr. at 35-36)

- Nothing in the claims suggests that the inhibitor and biologically active agent *are* chemically attached.

Second, the specification also supports CytomX's proposal in various ways. In that regard:

- The first two sentences of the Abstract read: "The invention relates to *molecules inhibiting biologically active compounds* and further comprising moieties specifically cleavable by a reagent produced by a target cell. The invention relates to inhibitors that bind, inhibit, suppress, neutralize, or decrease activity of a biologically active agent." ('504 patent, Abstract (emphasis added)) This wording strongly suggests that inhibitors are stand-alone "molecules" and that they inhibit separate "molecules" (the "biologically active compounds," which is a synonym for "biologically active agents").

- The specification describes the "[i]nhibitor-ligand pair"[4] as a "*set of molecules* that demonstrate specific binding[.]" ('504 patent, col. 5:36-37 (emphasis added); *see also* D.I. 51 at 10; D.I. 61 at 2) The reference to a "set of molecules" again denotes that this "pair" being described must amount to more than one molecule—not that the inhibitor and the ligand are part of the *same molecule*.

- Vytacera's counsel acknowledged that all of the examples described in the specification discuss how the inhibitor and biologically active agent are bound together, but do not discuss the two entities being chemically attached in the same molecule. (Tr. at 107)

For the above reasons, the term "inhibitor" should be construed to mean "a molecule, separate from the [biologically active agent/antibody], having the ability to bind, inhibit, suppress, neutralize, or decrease activity of a [biologically active agent/antibody]."

B. "inhibitor is administered alone or together with said antibody"

The second disputed term, "inhibitor is administered alone or together with said antibody" appears, *inter alia*, in claims 1 and 22 of the '913 patent, which are reproduced below:

> **1.** A method of site specific activation of an antibody comprising administration of an inhibitor which is deactivatable by a protease produced by a target cell comprising:
>
> (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of said antibody wherein said first moiety is operably linked to
>
> (b) a second moiety comprising a polypeptide specifically cleavable by said protease produced by said target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding, inhibiting, suppressing, or neutralizing activity of said inhibitor and restoration of activity of said antibody;

[4] The specification notes that the terms "ligand" and "[b]iologically active agent" "can be used interchangeably[.]" ('504 patent, col. 5:45-47; *see* D.I. 61 at 2 n.2)

said *inhibitor is administered alone or together with said antibody* such that the activity of said antibody is reduced until it reaches said target cell producing said protease wherein the inhibitor is cleaved by said protease and activity of said antibody is restored.

. . .

22. A method of site specific activation of a monoclonal antibody, a bispecific antibody and a single chain antibody or a combination thereof comprising administration of an inhibitor which is deactivatable by a reagent produced by a target cell comprising:

(a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof wherein said first moiety is operably linked to

(b) a second moiety comprising a polypeptide specifically cleavable by said reagent comprising a protease produced by said target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding, inhibiting, suppressing, or neutralizing activity of said inhibitor and restoration of activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof;

said *inhibitor is administered alone or together with said* monoclonal *antibody*, bispecific antibody and single chain antibody or a combination thereof such that the activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof is reduced until it reaches said target cell producing said reagent wherein the inhibitor is cleaved by said reagent and activity of said monoclonal antibody, bispecific antibody and single chain antibody or a combination thereof is restored.

('913 patent, cols. 85:22-39, 86:55-87:16 (emphasis added)) The parties' proposed constructions are below:

Term	**Vytacera's Proposal**	**CytomX's Proposal**

"inhibitor is administered alone or together with said antibody"	"[i]nhibitor can be attached to the antibody or not attached to the antibody"	"inhibitor [as construed] is administered by itself, i.e., not with said antibody, or inhibitor [as construed] is co-administered with said antibody"

(D.I. 43 at 8)

The dispute as to this term is an offshoot of the dispute regarding the construction of "inhibitor." The import of Vytacera's proposal here was (again) to obtain a construction that makes it clear that in some circumstances, an inhibitor can be "attached" (i.e., chemically attached, as part of the same molecule) to the antibody (i.e., the biologically active agent). (D.I. 53 at 11-12; D.I. 58 at 5-6; D.I. 61 at 7; *see also* Tr. at 83 (Vytacera's counsel noting that the dispute over this term involves "everything that we've been arguing previously [as to the 'inhibitor' term]")) For the reasons set out above regarding the "inhibitor" term, the Court has explained why this is incorrect. Nor does it make any sense to the Court to have that "chemical attachment" fight with regard to this particular claim term, which is about the entirely different concept of "administ[ration]" of the inhibitor and biologically active agent. (Tr. at 92-93 (CytomX's counsel noting that "it doesn't make sense to take the word 'administered' . . . and to convert it into kind of a compositional feature of attachment")) So for all of these reasons, the Court rejects Vytacera's proposed construction.

If "administering [the inhibitor] . . . together with" the antibody does not mean that the two can be chemically attached, then what does that language mean? In the Court's view, CytomX is correct to say that it means that the inhibitor is simply "co-administered with [the] antibody." The '913 patent specification says that "[i]n [a] preferred embodiment of the invention, the inhibitor is administered alone, *co-administered with* an active agent, or *co*[-]*administered with* an active agent and an adjuvant, a pharmaceutically acceptable carrier, a

diluent, or an excipient to a vertebrate." ('913 patent, col. 14:59-63 (emphasis added); *see* D.I. 51 at 12) And other portions of the specification emphasize that when two substances are administered "together," or co-administered, that just means that the two substances are provided to a patient "in combination with" each other in some way. ('913 patent, col. 37:4-5; *see also id*., cols. 5:44-48; 33:53-55)

For the above reasons, then, the term "inhibitor is administered alone or together with said antibody" should be construed to mean "inhibitor is administered by itself, i.e., not with said antibody, or inhibitor is co-administered with said antibody."

C. "reduction of binding activity of said inhibitor"

The third disputed term, "reduction of binding activity of said inhibitor," appears, *inter alia*, in claim 1 of the '504 patent. The claim is reproduced again here:

> **1**. An inhibitor which is deactivatable by a reagent produced by a target cell comprising:
>
> > (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of a biologically active agent wherein said first moiety is operably linked to;
> >
> > (b) a second moiety specifically cleavable by a protease produced by a target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes *reduction of binding activity of said inhibitor*.

('504 patent, col. 83:11-20 (emphasis added)) The parties' proposed constructions are below:

Term	**Vytacera's Proposal**	**CytomX's Proposal**
"reduction of binding activity of said inhibitor"	"[i]nhibition, suppression, or neutralizing activity of the inhibitor is reduced, lowered, or removed"	"a reduction in the inhibitor's ability to bind a biologically active agent"

(D.I. 43 at 4-5)

The crux of the dispute here is whether "reduction of binding activity" only dictates reduction of *binding activity* (as CytomX proposes), or whether (as Vytacera proposes) it also requires diminution of the inhibition, suppression or neutralizing activity of the inhibitor. In Vytacera's view, "binding" is basically a synonym for "inhibition, suppression, or neutralizing activity[,]" (Tr. at 113, 120), and so when the term-at-issue requires a "reduction of binding activity," that necessarily means not only a "reduction of binding activity" but also a reduction of "inhibition, suppression, or neutralizing activity." In CytomX's view, however, there is a difference between the "concepts of binding on the one hand," and "the other words of activity used in the claim [like] inhibit[s], suppress[es and] neutralize[s.]" (*Id*. at 121; *see also id*. at 123-24)[5]

Looking first at the words of claim 1, we see that limitation (a) uses the conjunction "or" in describing how the first moiety interacts with the biologically active agent. The use of "or" would typically indicate that the first moiety "binds" the agent, *or* "inhibits" the agent, *or* "suppresses" the agent, *or* "neutralizes" the agent *or* "decreases activity of" the agent, *or* that it *can* do more than one or all of these things—but it would not typically suggest that the first moiety is *required to* do any more than one of these things. That said, limitation (b) requires that cleavage of a second moiety causes reduction of the "*binding* activity" of the inhibitor. In light of that language in limitation (b), both parties agree the first moiety is at least required to *bind* a biologically active agent. (D.I. 51 at 13; Tr. at 121, 126-27, 131, 142)

[5] This is because, in CytomX's view, while binding "implies necessarily a decrease in activity or a suppression of activity" or a neutralization of activity in a certain way, a moiety may also inhibit or suppress or neutralize activity in a "different way than binding" does. (Tr. at 128) In other words, to CytomX, "inhibits, suppresses, [and] neutralizes" are broader terms than binding, vis-à-vis the inhibitor's impact on a biologically active agent.

From there, in the Court's view, the fact that the claim uses separate terms for "binds," "inhibits," "suppresses," "neutralizes," or "decreases activity" indicates to the Court that those are each at least somewhat different processes, and that (contrary to Vytacera's position) they do not all have the exact same meaning. *See Helmsderfer v. Bobrick Washroom Equip., Inc*., 527 F.3d 1379, 1382 (Fed. Cir. 2008) ("Our precedent instructs that different claim terms are presumed to have different meanings."). And because of the use of the word "or" in limitation (a), even though the first moiety is required to bind a biologically active agent, it does not appear that the moiety is also necessarily required to inhibit, or suppress, or neutralize or decrease the activity of the agent (at least to an extent different from what occurs during "binding" activity). The claim seems to allow that the first moiety *can* do one or more of those things in addition to binding with the agent, but that it is not *required* to do any of them. And so, when it comes to the term in question, Vytacera's proposal appears to contravene the claim language—in that it would require that cleavage of the second moiety cause not only reduction of *binding* activity (i.e., the kind of reduction specifically called out by the claim term itself), but also an additional type of reduction of *inhibition, suppression or neutralizing* activity, when the claim does not actually require that any such additional activity would have been occurring in the first place.

In addition to the claim language, the '504 patent's prosecution history provides some support to CytomX's position. In response to an Office Action—wherein the Examiner had rejected the proposed claims pursuant to 35 U.S.C. §§ 102 & 103 in light of prior art including "Thorpe et al."—the patentee amended limitation (b) in claim 1. (D.I. 43, ex. 1) In doing so, the patentee removed the terms "inhibiting, suppressing, or neutralizing" from that part of the claim, as follows:

> (b) a second moiety specifically cleavable by a protease ~~reagent~~ produced by a target cell, wherein said first and second moieties

> are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding~~, inhibiting, suppressing, or neutralizing~~ activity of said inhibitor.

(*Id*. at Appx0008 (alteration and emphasis in original)) In further explaining his position, the patentee responded to the Examiner's rejection by noting, *inter alia*, that:

> Thorpe et al. disclose[s] a site specific delivery of a coagulant using an antibody. Thorpe et al. does not disclose "a specific cleavage of said second moiety causes reduction of binding activity of said inhibitor to its target." Thorpe et al. fusion protein constructs are cleaved without affecting the protein activity or the binding activity.

(D.I. 43, ex. 1 at Appx0003 (regarding 35 U.S.C. § 102 rejection); *see also id*. (regarding 35 U.S.C. § 103 rejection)) It is hard to tell for sure what was in the patentee's mind here, or how or whether the patentee felt that striking "inhibiting, suppressing, or neutralizing activity" from limitation (b) helped underscore why the present invention should be distinguished from Thorpe et al.[6] But in the end, the effect of the amendment seems to be that after cleavage, no associated reduction of "inhibiting, suppressing, or neutralizing" activity (other than what may occur due to a reduction in binding activity) is relevant to the claim's scope.[7] (Tr. at 133) And so (as

[6] During the *Markman* hearing, Vytacera's counsel suggested that in distinguishing the claim from Thorpe et al. during prosecution, the only thing that the patentee was trying to convey to the Examiner was that in Thorpe et al. "nothing happened with the cleavage[,]" while in the patented invention "once you cleave the inhibitor, it has a reduction of binding activity." (Tr. at 115) But the Court then followed up by asking counsel why—if all the patentee was trying to do was to make that point—did the patentee remove the words "inhibiting, suppressing, or neutralizing" from the claim? (Tr. at 116) After all, if those words are simply synonyms for "binding," as Vytacera suggests, then there would seem to be no reason to remove them from the claim—since their presence in the claim would not interfere with the point the patentee was trying to make. Vytacera's counsel did not have an answer to that question. (*Id*.)

[7] The Court need not decide if this evidence is so clear and unmistakable to amount to prosecution disclaimer. *TC Tech. LLC v. Sprint Corp*., 379 F. Supp. 3d 305, 325 (D. Del. 2019). The Court simply cites to it as another piece of persuasive evidence indicating that CytomX's proposed construction is correct.

Vytacera's counsel acknowledged during the *Markman* hearing), its proposed construction amounts to an effort to re-insert into the claim the very thing that the patentee struck from the claim during prosecution. (Tr. at 140-41) That seems inappropriate.

For the reasons set out above, Vytacera's proposed construction should not be adopted. Having said that, the Court does not think that adopting CytomX's proposed construction is necessary either. CytomX's proposal simply repositions the words of the claim term, which will not be helpful to the factfinder. (D.I. 58 at 6) Thus, having resolved the parties' dispute here, the Court will not recommend a new construction. Instead, it simply recommends that "reduction of binding activity of said inhibitor" be afforded its plain and ordinary meaning.

D. "biologically active agent"

The fourth and final disputed term, "biologically active agent" also appears in claim 1 of the '504 patent. One more time, that claim reads:

> **1**. An inhibitor which is deactivatable by a reagent produced by a target cell comprising:
>
> > (a) a first moiety that binds, inhibits, suppresses, neutralizes, or decreases activity of a *biologically active agent* wherein said first moiety is operably linked to;
> >
> > (b) a second moiety specifically cleavable by a protease produced by a target cell, wherein said first and second moieties are not attached in nature and wherein specific cleavage of said second moiety causes reduction of binding activity of said inhibitor.

('504 patent, col. 83:11-20 (emphasis added)) The parties' proposed constructions are below:

Term	**Vytacera's Proposal**	**CytomX's Proposal**
"biologically active agent"	"[m]olecules that regulate the immune response to disease cells including stimulation of cells to secrete immune-augmenting cytokines,	"biologically active compound, which is a separate molecule from the inhibitor"

	chemokines, an inhibitory peptide"	

(D.I. 43 at 3)

The Court first examines CytomX's proposed construction. That proposal imports the phrase "biologically active compound," which the parties all agree means the same thing as "biologically active agent." (Tr. at 160-61, 176-77) In the Court's view, this part of CytomX's construction could be confusing, because it might suggest that "biologically active compound" is the only synonym for "biologically active agent" used by the patents. In fact, that is not so, as the patents also use other terms (like "ligand") to mean "biologically active agent." (*See, e.g.*, '504 patent, col. 5:45-47) So the Court is not going to adopt that part of CytomX's proposal.

The only remaining part of CytomX's proposal relates to the chemical "separateness" of the inhibitor from the biologically active agent. (D.I. 51 at 15) The Court has already resolved that dispute above in addressing the term "inhibitor." There is no need to do so again here by importing this additional proposed language (i.e., "which is a separate molecule from the inhibitor") into a new construction of "biologically active agent."

This is all a way of saying that the Court does not find CytomX's proposal very helpful in resolving the parties' true dispute over this term. Vytacera's proposal does at least engage with that dispute, and the Court addresses it next.

Vytacera's proposal is taken from the following excerpt in the specification:

> Biologically active agent, active agent, (biologically) active compound, biological response modifier, or ligand (can be used interchangeably): Are *molecules that regulate the immune response to disease cells including stimulation of cells to secrete immune-augmenting cytokines, chemokines, a[n] inh[i]bitory peptide*, molecules like interleukines (IL), IL-1, IL-2, GM-CSF, IFN, and IL-12, colony stimulating factor (CSF), GM-CSF, interleukins, interferons, colony stimulating factors, a coagulation factor, a fibrinolytic protein, a photosensitizing agent, or an

> imaging agent, a biological activation cascade or a component of this cascade, a component of the coagulation system, a component of fibrinolysis system, a component of the complement system, the kinin system, an enzyme which converts the inactive precursor of a pharmacological substance into the pharmacologically active substance, antibodies, peptides, muteins of the above, a pharmacologically active substance, macromolecular drugs, chemical drugs, and the like are contemplated.

('504 patent, col. 5:45-62 (emphasis added)) Vytacera considers this block quote (hereafter, "the block quote") to be a definition of "biologically active agent"; it urges the Court to adopt only the portion of that asserted definition that is italicized above. But the Court does not think it should do so, for a few reasons.

As an initial matter, while the above-excerpted block quote does seem an attempt by the patentee to explain what a "biologically active agent" can be, the Court is not convinced that Vytacera's proposal (which reproduces only a portion of that block quote) is faithful to the meaning of this text. Vytacera's position is that the block quote is meant to explain that "biologically active agents" are all "molecules that regulate the immune response to disease cells"; it argues that everything listed after this wording in the block quote are simply examples of molecules that regulate the immune response. (Tr. at 149, 151, 155, 187-89) The Court, however, is not sure that is correct. For example, CytomX's counsel argued that one of those listed agents—"photosensitizing agents"—do *not* regulate the immune response to disease cells. (D.I. 51 at 16; Tr. at 180-81) In its briefing, CytomX pointed to a portion of the specification that describes these photosensitizing agents; that text seems to focus on how such agents absorb light and transfer absorbed energy to oxygen molecules in tissue. (D.I. 51 at 16 (citing '504

patent, col. 32:10-28)) The text does not appear to indicate (at least facially) that such agents in fact regulate an immune response. (*Id.*)[8]

Instead, the Court believes that CytomX's reading of the block quote is the better one. CytomX asserts that the block quote is simply delineating exemplary biologically active agents (that is, agents that have some biological activity on living matter), and that it does so, for the most part, by listing various such agents and setting them off by commas. (Tr. at 178-79) In other words, CytomX reads this listing as follows:

> Biologically active agent, active agent, (biologically) active compound, biological response modifier, or ligand (can be used interchangeably): Are[:]
>
> [(1)] molecules that regulate the immune response to disease cells including stimulation of cells to secrete immune-augmenting cytokines,
>
> [(2)] chemokines,
>
> [(3)] a[n] inhibitory peptide,
>
> [(4)] molecules like interleukines (IL), IL-1, IL-2, GM-CSF, IFN, and IL-12,
>
> [(5)] colony stimulating factor (CSF),
>
> [(6)] GM-CSF,
>
> [(7)] interleukins,
>
> [(8)] interferons,
>
> [(9)] colony stimulating factors,

[8] During the *Markman* hearing, Vytacera's counsel stated that it would point the Court to text in the specification that showed that a photosensitizing agent *does* affect the immune response to disease cells. (Tr. at 189-90) But its counsel ended up citing to the same portion of the specification that CytomX pointed to (discussed above). (*Id*. at 195) And the Court did not understand Vytacera's counsel's argument as to how that part of the specification supported Vytacera's argument. (*Id*.) There might be other evidence that suggests that Vytacera is right here, but Vytacera has not presented it to the Court.

> [(10)] a coagulation factor,
>
> [(11)] a fibrinolytic protein,
>
> [(12)] a photosensitizing agent, or an imaging agent,[9]
>
> [(13)] a biological activation cascade or a component of this cascade,
>
> [(14)] a component of the coagulation system,
>
> [(15)] a component of fibrinolysis system,
>
> [(16)] a component of the complement system,
>
> [(17)] the kinin system,
>
> [(18)] an enzyme which converts the inactive precursor of a pharmacological substance into the pharmacologically active substance,
>
> [(19)] antibodies,
>
> [(20)] peptides,
>
> [(21)] muteins of the above,
>
> [(22)] a pharmacologically active substance,
>
> [(23)] macromolecular drugs,
>
> [(24)] chemical drugs,
>
> [(25)] and the like are contemplated.

(*See* '504 patent, col. 5:45-62) This interpretation seems sensible. And it does not appear disputed that all of the above-listed substances would at least qualify as agents that have some biological activity (i.e., "biologically active agents").

Another point in favor of CytomX's position is that, in other portions of the specification that describe preferred embodiments, the patent clearly states that substances including "vitamins" and "toxins" are also biologically active agents. ('504 patent, col. 27:36-59 (noting

[9] According to Vytacera's counsel, these are one in the same. (Tr. at 188-89)

that "vitamins" are an example of "ligands"); *id*., cols. 5:65-6:1, 28:49-50 (stating that "toxins" are "active agents" and that they are inhibited by an inhibitor)) This would be in harmony with CytomX's reading of the block quote, since at the end of that quote, the patent notes that the above list of biologically active agents is not exclusive (by using the wording "and the like"). ('504 patent, col. 5:62) But it would not jibe with Vytacera's reading of the block quote. During the *Markman* hearing, Vytacera's counsel confirmed that in Vytacera's view, "vitamins" and "toxins" are *not* biologically active agents and would *not* fit within the confines of its proposed construction. (Tr. at 157-59) That simply indicates to the Court that Vytacera's proposed construction must be wrong—because it would directly contradict those portions of the specification that say that "vitamins" and "toxins" *are* biologically active agents.

So the Court has clearly resolved the dispute as to Vytacera's proposed construction—by rejecting it. And it has explained why it found CytomX's proposed construction unhelpful. In light of this, and because the meaning of the term-at-issue seems not hard to discern (it is an agent, that has some amount of biological activity), (D.I. 51 at 15; Tr. at 172-73; ('504 patent, cols. 3:57-58, 83:13), the Court recommends that "biologically active agent" simply be afforded its plain and ordinary meaning.

IV. CONCLUSION

For the foregoing reasons, the Court recommends that the District Court adopt the following constructions:

1. "inhibitor" should be construed to mean "a molecule, separate from the [biologically active agent/antibody], having the ability to bind, inhibit, suppress, neutralize, or decrease activity of a [biologically active agent/antibody]";

2. "inhibitor is administered alone or together with said antibody" should be construed to mean "inhibitor is administered by itself, i.e., not with said antibody, or inhibitor is co-administered with said antibody";
3. "reduction of binding activity of said inhibitor" should be afforded its plain and ordinary meaning; and
4. "biologically active agent" should be afforded its plain and ordinary meaning.

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The failure of a party to object to legal conclusions may result in the loss of the right to *de novo* review in the district court. *See Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987).

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website, located at http://www.ded.uscourts.gov.

Dated: October 7, 2021

Christopher J. Burke
Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE